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Page

Social Irresponsibility in Science 513

The Great Greenhouse Scare 514

Who would Live in California ? 515

OLD WORLD

Computers / Population / Technological Forecasting / Chemicals/Cancer Research/Nuclear Power/Miscellaneous Intelligence/Parliament in Britain . . 516

Select Committee probes Embarrassing Area . . 519

NEW WORLD

Earthquakes trigger Reports but no Funds/Seismology/Latent Lunar Seismology/Target for Apollo 15 . 520

NEWS AND VIEWS

Isolation of the Cholinergic Receptor Protein/Aftermath of the Revolution/Earthquakes/Arctic Geology/Pulsar Models/Bacteriophages 523

Marriage and Fertility in Academic Life—HUDSON and JACOT (Edinburgh) 531

Pozzuoli Event in 1970—YOKOYAMA (Hokkaido) . 532

Uses of Artificial Insemination—JONES (Zoological Society of London) 534

Geotectonics—Evolution of Kenya Rift Valley—BAKER and WOHLENBERG (Nairobi) 538

Biochemical systems—Parameter sensitivity as a criterion for evaluating and comparing performance — SAVAGEAU (Michigan) 542

X-ray astronomy—Variable emission from M87—BYRAM, CHUBB and FRIEDMAN (US Naval Research Laboratory) 544

LETTERS TO *NATURE*

Physical Sciences

Gravitational radiation—Possible new means of detection—ANDERSON (Uppsala) 547

Cosmic rays—Acceleration mechanisms and abundances—HAVNES (Utrecht) 548

Environment—Decrease in clear air transmission above Los Angeles—HODGE (Seattle) 549

Page

Rock shear waves—Propagation anisotropies and seismic studies—CHRISTENSEN (Seattle) . . . 549

Oceanography—Measurement of tilt of a frozen sea—WEBER (Canada Department of Energy, Mines and Resources) and LILLESTRAND (Control Data Corporation) 550

Earth's crust—Central part of Baffin Bay is oceanic—BARRETT, KEEN, MANCHESTER and ROSS (Bedford Institute, Nova Scotia) 551

Supernovae—Connexion with extinction of dinosaurs—RUSSELL (National Museum of Natural Sciences, Ottawa) and TUCKER (American Science and Engineering) 553

Biological Sciences

Cholinergic receptors—Isolation of membrane protein to which toxin binds in electric tissue of *Torpedo*—MILEDI, MOLINOFF and POTTER (London) . 554

Retina—Differential response of ganglion cells to images in or out of focus—IKEDA (London) and HILL (Ohio State) 557

Retinal pigments—Implications of torsional potential of isomers for visual excitation—HONIG and KARPLUS (Harvard) 559

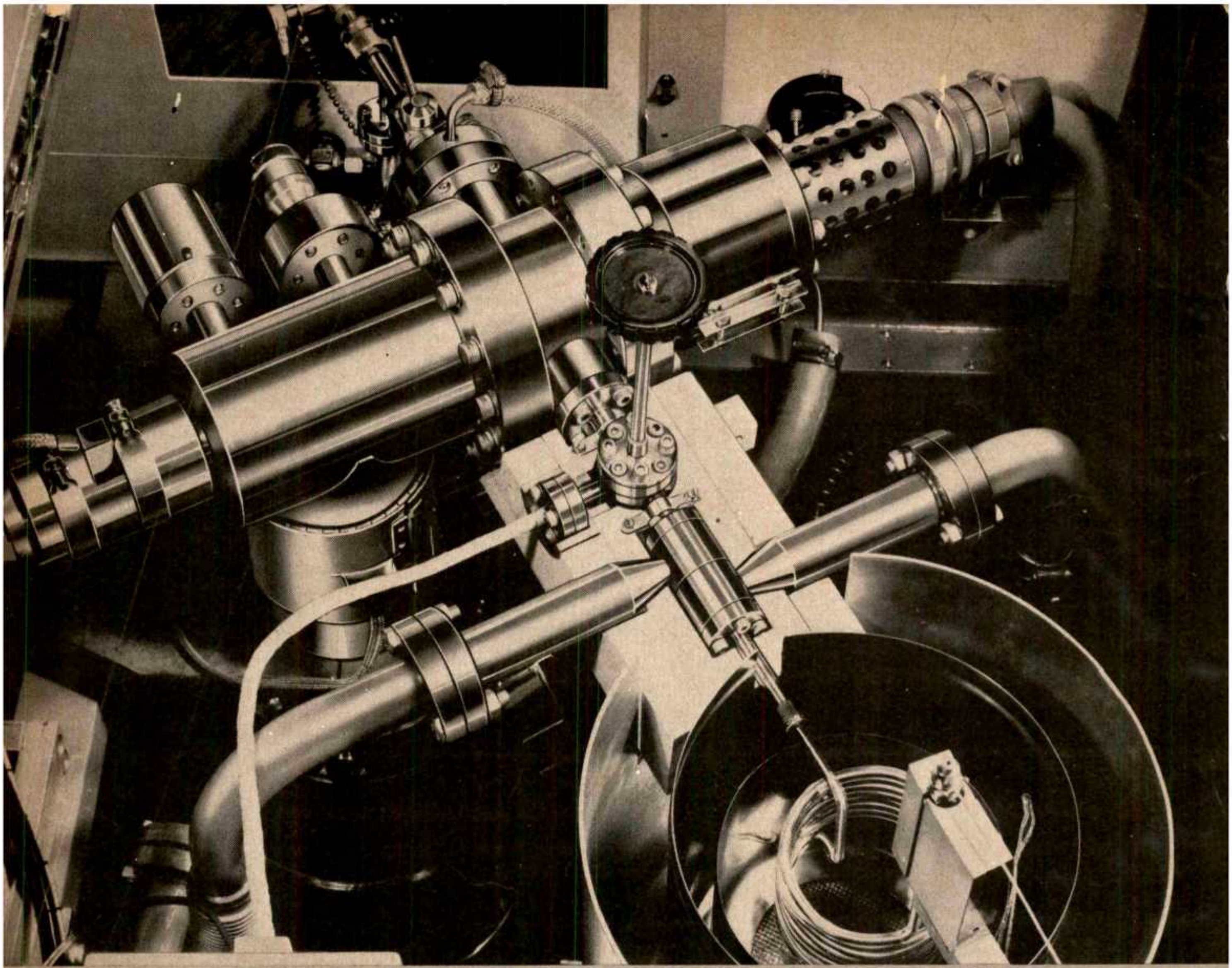
Cornea—Renewal of epithelium from pericorneal papillar structure—DAVANGER and EVENSEN (Makerere) 560

Vision—Estimating the time of juncture of an object with an observer—WEINBERGER (National Physical Laboratory of Israel) 562

Adrenal enzymes—Neural stimuli regulate adrenal enzymes that evoke attack behaviour—REIS, MOORHEAD, RIFKIN (Cornell), JOH and GOLDSTEIN (New York) 562

L-Asparaginase—Duration of *in vivo* effects on experimental metastasis—FIDLER (Pennsylvania) . . 564

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 525 to 530



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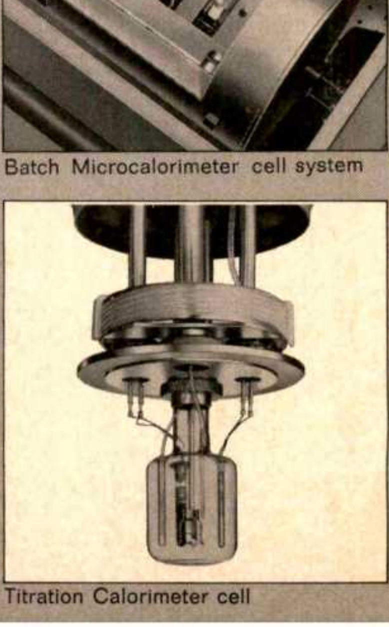

Titration Calorimeter cell

Page

MLV—Method of detection and quantitation of murine leukaemia viruses—BASSIN, TUTTLE and FISCHINGER (US National Institutes of Health) . 564

Lymphocytes—Participation of θ-bearing cell in an *in vitro* assay of transplantation immunity—LONAI, CLARK and FELDMAN (Weizmann Institute of Science) 566

Prostaglandin—$F_{2\alpha}$ induces lactogenesis and abortion in pregnant rats—DEIS (Cordoba) 568

Penicillium—Lytic plaques produced by viruses—BORRÉ, MORGANTINI, ORTALI and TONOLO (Rome) 568

Glycolipid synthesis—Decrease in virus transformed cells could result from loss of contact inhibition—ROBBINS and MACPHERSON (Imperial Cancer Research Fund) 569

Chromosomes—Univalents segregate on separate spindle at meiosis—FORD (Sydney) 570

Chlorinated hydrocarbons—Effect on medullary bone formation in birds—OESTREICHER, SHUMAN and WURSTER (New York) 571

Page

Leaves—New method for measuring surface area—THOMPSON and LEYTON (Oxford) 572

Fog—Echolocation by bats—PYE (London) . . 572

Soil—Accurate determination of acidity of soil water—DOEMEL and BROCK (Indiana) 574

BOOK REVIEWS

by Paul Gary Werskey, C. D. Darlington, I. K. Ferguson, Duncan Murchison, J. P. Quilliam, Keith Oatley, E. G. Gray, James A. Barnett 575

CORRESPONDENCE

PhD Theses (L. Beverly Halstead)/Dowsing (Dorothy Emmet) 579

Obituary Professor A. Ghigi/Academician A. I. Mikoyan 579

Announcements/University News/Appointments/Miscellaneous 580

Next Monday's issue will include

Glass surface cracks—Hertzian fracture data and a new analytical method—POLONIECKI and WILSHAW (Sussex)

Stars—Why some elements are overabundant in Ap stars—WATSON (Cornell)

X-ray astronomy—Position of Cen XR-2, April 1967—FRANCEY (Tasmania)

Solar–terrestrial relations—A negative sudden phase anomaly—OHSHIO (Radio Research Laboratories, Tokyo)

Seismology—Deep seismic reflexions from random data—MERZER (Cambridge)

Next Wednesday's issue will include

Protein synthesis—Initiation of adenovirus proteins—CAFFIER, RASKAS, PARSONS and GREEN (Saint Louis)

Virology—Evidence that leukaemic viruses act as helpers for spleen focus-forming virus—ECKNER and STEEVES (Roswell Park Memorial Institute)

Vaccination—BCG vaccine confers resistance to Friend disease virus in mice—LARSON, USHIJIMA, FLOREY, BAKER and BAKER (Montana)

Polysomes—Regulation by insulin and amino-acids in liver—EKREN, JERVELL and SEGLEN (Oslo)

X-rays—Removal of bases from nucleic acid after radiation—HARIHARAN and CERUTTI (Princeton)

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Page

Pollution in its Place 583

Teaching without Research 584

OLD WORLD

Royal Commission Provides Framework for Study/CERN/Chemistry/Computer Policy/Sakharov's Rights/Parliament in Britain 586

NEW WORLD

Nixon and Kennedy Peddle Rival Cancer Cures/Salaries of US Scientists in 1970/Udall praises NAS/Computers 590

NEWS AND VIEWS

Human Breast Cancer Virus?—Bright Future for European Particle Physics/Trilobites/Rodenticides/Reservoirs/Protein Synthesis/Stromateoid Fishes/Nuclear Physics/Ocean Floors/Selenology 593

Problems facing University Science—JEVONS (Manchester) 601

Defence of the Berkeley Work on Alpha-Emitting Isotopes of Element 104—GHIORSO, NURMIA, HARRIS, ESKOLA and ESKOLA (California) 603

Ageing of Mammals—BULLOUGH (London) . . 608

Cancer—Search for a human breast cancer virus—MOORE, CHARNEY, KRAMARSKY, LASFARGUES, SARKAR (Institute for Medical Research, NJ), BRENNAN, BURROWS (Michigan Cancer Foundation), SIRSAT, PAYMASTER and VAIDYA (Tata Memorial Center, Bombay) 611

Visual preferences—For colour and brightness in rhesus monkeys—HUMPHREY (Oxford) 615

LETTERS TO *NATURE*

Physical Sciences

Seismology—Natural Earth oscillations by cryogenic gravity meter—TUMAN (Stanislaus State College) . 618

Doppler velocity—Measurements using white light—SCHWAR (London) 621

Antarctic cirques—Some may be of Tertiary age—SELBY and WILSON (Waikato) 623

Page

Drag—Clusters of submicron spheres in gravitational and electrical fields—MEGAW and WELLS (AERE, Harwell) 624

Fluorine—Decomposition and pyrohydrolysis methods of estimation compared—KAKABADSE, MANOHIN, BATHER, WELLER and WOODBRIDGE (Manchester) 626

Biological Sciences

Breast cancer—Cross-antigenic relationship between mouse and human tumour viruses—CHARNEY and MOORE (Institute for Medical Research, NJ) . 627

Cerebral cortex—Localization of ^{3}H-GABA by electron microscopic autoradiography—BLOOM and IVERSEN (Cambridge) 628

Anti-lymphocyte serum—Preparation of highly radioactive bovine anti-mouse lymphocyte antibody—DRESSER (MRC, Mill Hill) 630

Cancer—*In vitro* assay of leukocyte migration inhibitory factor—WOLBERG and GOELZER (Wisconsin) . 632

Cell-mediated immunity—Lentinan as an immuno-accelerator—MAEDA and CHIHARA (National Cancer Centre, Tokyo) 634

Immunology—Private and public H-2 antigens of mice—KLEIN (Michigan) 635

Evolution—Denial of Anderson's viral hypothesis—WEST (Virginia Polytechnic Institute) . . . 637

Drugs—Hypnotics and hangover effects—WALTERS and LADER (London) 637

BOOK REVIEWS

by F. S. Dainton, Paul Gary Werskey, N. W. Pirie, C. D. Pigott, John Gribbin, Ronald Girdwood, C. D. Green, K. A. McLauchlan, Duncan Murchison . . . 639

Obituary—Dr G. A. Reay/Academician A. I. Alikhanov 643

Announcements/University News/Appointments/Miscellaneous/International Meetings 643

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 595 to 600

(Continued overleaf)

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Page

Computers, Conservatives and Governments . . 1

How will the Universities be Nourished ? 2

Who will Referee the Referees ? 3

OLD WORLD

Select Committee Computes ICL's Future/Universities/Cancer Therapy/ESRO/Corrosion/Nuclear Energy/Countryside/Parliament in Britain 4

NEW WORLD

Sweetness and Light Break Out Again/Congress/NASA/Arms Race 8

NEWS AND VIEWS

Polywater Drains Away/The DNA Replication Mystery/What Turns Plants On ?/Exploration/Acarology/Ribosomes / Chemical Carcinogens / Nutrition / Pollution/ Radio Galaxies/Nucleation 11

Psychobiological Studies of Aggressive Behaviour—HAMBURG (Stanford) 19

Role of the Research Councils—GRAY (MRC) . . 23

Antimatter—Possible aggregations in the universe—OMNES (Paris-Sud) 26

Palaeomagnetism—Effect of oxidation of the natural remanent magnetization of titanomagnetite in suboceanic basalt—MARSHALL and COX (Stanford) 28

Polywater—Contaminants probably responsible for the phenomenon—BARNES, CHERRY, FINNEY and PETERSEN (London) 31

DNA polymerase—Purification of an altered enzyme from an *E. coli pol* mutant strain—KELLEY and WHITFIELD (Edinburgh) 33

Transfer RNA—New species which participates in peptidoglycan synthesis but not in protein synthesis—STEWART, ROBERTS and STROMINGER (Harvard) 36

LETTERS TO *NATURE*

Physical Sciences

Binary stars—Ways to study collapsars and neutron stars—WOOLF (Minnesota) 39

Solar system—Observed abundance distribution of chemical elements as a test of Alfvèn's theory of its origin—HAUGE (Oslo) 39

Metrology—Pyrolytic graphite in X-ray microcalorimeter—KEMP, MARSH and BAKER (NPL) . 41

Earth's crust—Convection plumes in the lower mantle—MORGAN (Princeton) 42

Pingos—Occurrence in southern Ireland—MITCHELL (Trinity College, Dublin) 43

Oil pollution—Solubility of crude oils and kerosene in seawater—BOYLAN and TRIPP (Woods Hole Oceanographic Institution) 44

Stratosphere—Warming observed by Nimbus 4—BARNETT, HARWOOD, HOUGHTON, MORGAN, ROGERS, WILLIAMSON (Oxford), PECKHAM and SMITH (Heriot-Watt) . . . 47

Biological Sciences

Allografts—Tolerance may be mediated by serum-borne factors—HELLSTRÖM, HELLSTRÖM (Washington, Seattle) and ALLISON (Clinical Research Centre, Harrow) 49

Immunology—A marker antigen for lymphocytes derived from bone marrow—RAFF, NASE and MITCHISON (MRC, Mill Hill) 50

Sex chromosomes—Care needed when quinacrine fluorescence used to identify *Y*—BORGAONKAR and HOLLANDER (Johns Hopkins) 52

—Quinacrine used to determine the sex of a foetus—SHETTLES (Presbyterian Hospital, New York) 52

—Identification in amniotic fluid—ROOK, HSU, GERTNER and HIRSCHHORN (Mount Sinai School of Medicine, New York) . . 53

Brain—Metabolism of noradrenaline in rats affected by stress to their mothers during pregnancy—HUTTUNEN (Massachusetts General Hospital) . 53

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 14 to 18

(*Continued overleaf*

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Page

Vision—Movement after effect depends on patterned surround—DAY and STRELOW (Monash) . . 55

Phytochrome—There may be more than one "primary reaction"—MOHR, BIENGER and LANGE (Freiburg) 56

Phytoplankton—Net photosynthesis in a lake and diurnal oscillation in bacterial populations—SAUNDERS and STORCH (Michigan) 58

DDT—Food chain model for kinetics in a freshwater marsh—EBERHARDT (Battelle Memorial Institute), MEEKS (Winous Point Shooting Club, Ohio) and PETERLE (Ohio State) 60

Page

BOOK REVIEWS

by John Ziman, John Vaizey, Julia A. E. Hubbard, Derek Richter, M. J. Colbourne, John B. Free, D. J. Creasey, T. S. West 63

CORRESPONDENCE

Responsibility in Science (Peter Chapman, David Dickson, Shivaji Lal, Jerry Ravetz, Hilary Rose, Steven Rose, Jonathan Rosenhead, David Wield, Maurice Wilkins) 67

Announcements—Miscellaneous 67

Next Monday's issue will include

Gravitational waves—Effect on evolution of binary WZ Sagittae—VILA (Pennsylvania).

Solar system—Temperature of the Sun during its early history—KURODA (Arkansas).

Rare gases—Relationships between abundance pattern and isotope anomalies—KURODA, REYNOLDS, SAKAMOTO and MILLER (Arkansas).

Ice age—Radiocarbon chronology of deglaciation in Western Scotland—PEACOCK (Institute of Geological Science, Edinburgh)

Polymers—Effects of size and surface on creep—BENHAM and MALLON (Queen's University, Belfast)

Next Wednesday's issue will include

Haemoflagellates—Mechanism of resistance to purified acriflavin in *Leishmania tarentolae*—STRAUSS (Rockefeller)

Scrapie agent—Identification of an eclipse phase—FIELD, JOYCE and KEITH (Newcastle General Hospital)

Fucosterol—A metabolite of the tobacco hornworm—SVOBODA, THOMPSON and ROBBINS (US Department of Agriculture)

Lactate dehydrogenase—Hybridization in physiological *in vitro* conditions—MILLAR, SUMMERS and NIZIOLEK (US National Naval Medical Center)

Immunoglobulins—Genetic control of variable and constant regions of heavy chains—MAGE, YOUNG-COOPER and ALEXANDER (US National Institutes of Health)

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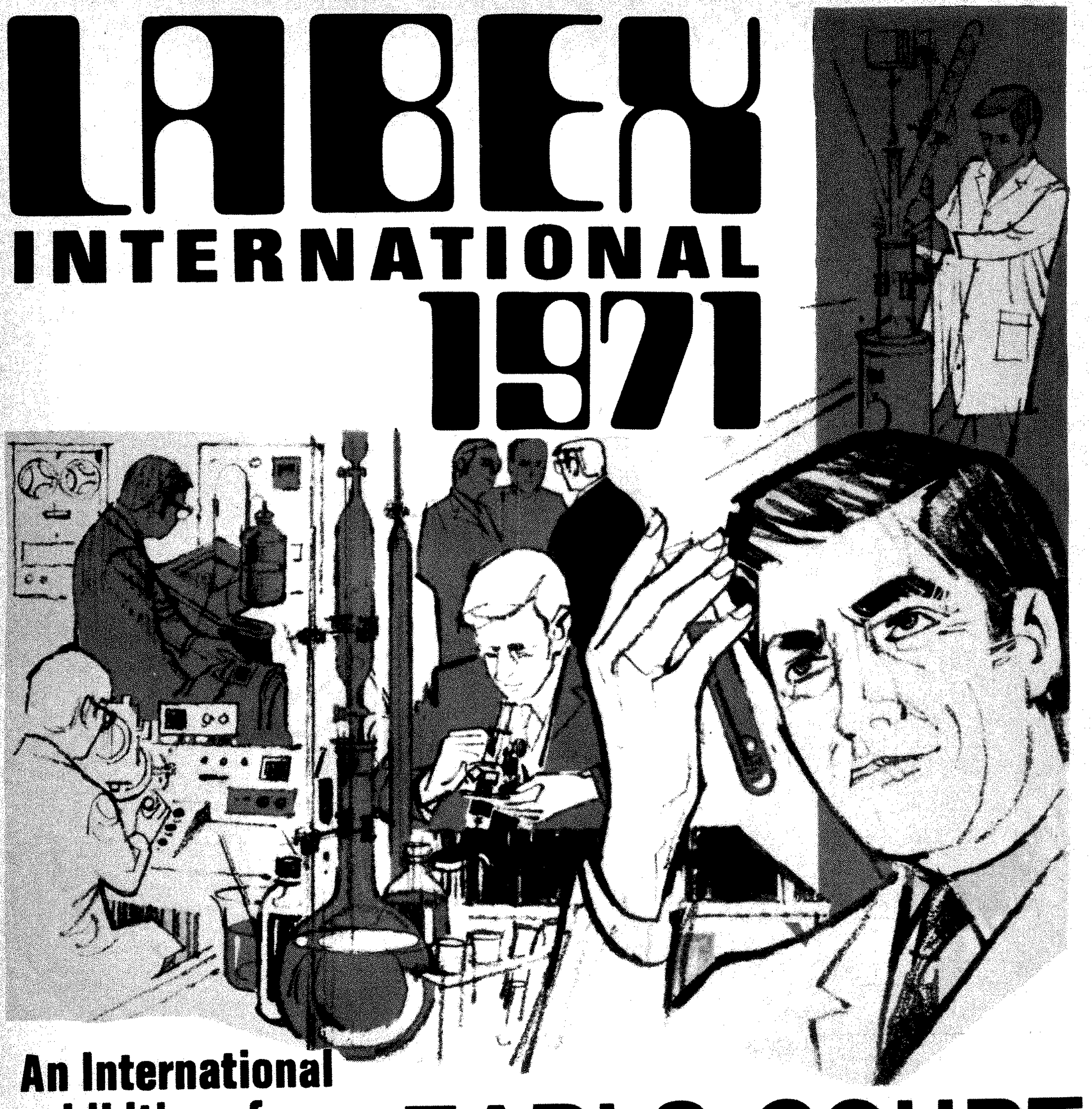

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Social Irresponsibility in Science

THE British Society for Social Responsibility in Science is perhaps more than other new organization in great need of that claim on public attention which the Americans call credibility. Everybody agrees, of course, that no harm can be done by a sober examination of some of the questions that sensible people must ask about some of the social problems occasioned by modern science and, more particularly, by modern technology. There is even a need that public attention should be drawn to some of these issues and to the general need for vigilance. In this sense, the British Society for Social Responsibility seemed to have a useful job to do when it began just over two years ago. Its difficulties since then seem to have stemmed largely from the problem of how to provide a commentary on current affairs which is at once lively and balanced.

The society's efforts so far have not been conspicuously successful. What might have been a valuable public discussion on the ethical problems of modern biology (see *Nature*, **228**, 900; 1970) seems to have tailed off into discussion of the process of radicalization of science and even some of the familiar problems of Vietnam. It is of course unavoidable that an organization like this should be seen as a vehicle for other causes than those included in the prospectus and in ordinary circumstances many scientists would be willing to forgive the society its errors of judgment and its excesses for the sake of what might be done.

It is therefore a great misfortune that the society should now have chosen to make an ass of itself in public over its relations—and in particular its lack of a formal relationship—with the British Association. At the last annual meeting of the British Association in Durham, members of the society created a stir, sometimes a healthy stir, by speaking up at public meetings, sometimes by interrupting public meetings and by organizing public spectacles of various kinds.

Since then the society has been debating within itself the principles on which its relations with the British Association should be determined and the outcome seems to be the decision not for the time being to cooperate with the association. This view is summarized in the current issue of *New Scientist* (February 11, 1971) by Mrs Hilary Rose, the new chairman of the society, who protests (quite legitimately) at the composition of the review committee trying to hammer out a role for the association in the years ahead (see *Nature*, **228**, 697; 1970) and then goes on to say that the society

> "would gladly cooperate with a rejuvenated BA to tackle the problems of the mutual impact of science and society. However, a virtual revolution in BA attitudes and practice is required. Without some concrete evidence that the BA at least realizes the magnitude of the task it faces, BSSRS will feel such cooperation to be futile. It would merely feed complacency, and weaken the impulse to reform."

As a part of the same solemn movement of protest, Dr J. R. Ravetz, one of the council of the British Society for Social Responsibility in Science, has taken the deliberate and weighty step of resigning from the association's innocent committee responsible for conducting the affairs of Section X. On the face of things at least, it looks as if diplomatic relations between the two bodies have been severed with all the pomp and dignity appropriate to political rows between the smaller sovereign states.

In all this, it is a great misfortune that the British Society for Social Responsibility in Science has so quickly given in to the temptation to pomposity which has so often in the past been one of the most serious deficiencies of the British Association. The truth is that a body which sets out to be an enlightened pressure group cannot safely afford the luxury of haughtiness. If Mrs Rose means what she says about the society's willingness to cooperate with a rejuvenated British Association, is it not a part of her colleagues' job to help to see that something they would welcome does actually emerge from the deliberations of the review committee, and from the decisions that will eventually be taken about the reorganization of the British Association ? If, on the other hand, the British Society for Social Responsibility in Science considers that it would itself be able to perform the contemporary work that the British Association could (and should) be doing, would it not be much more honest to say just that ? And would it not then be proper for the society to show that on some occasions at least it can provide the world not merely with the definitions of problems which it considers to be important but also, now and again, with some attempts at constructive solutions? With so much talk and so little work to show, the society has unknowingly as serious a problem on its hands as the British Association.

Postal Strike

THIS issue of *Nature* will be the first to be distributed outside North America and parts of the United Kingdom since the beginning of the British postal strike on January 20. Missing copies will be despatched as soon as the strike is over but there will unfortunately be some delay.

Until further notice, and certainly for some days after the strike is over, contributors and subscribers outside Britain should write only to the North American office of *Nature*, 711 National Press Building, Washington, DC 20004 (telephone 202 737 2355). Communications by telex may be sent either to Washington (64280) or to London (262024).

Manuscripts for publication which may eventually be accepted but which are at present embedded in the British postal system will not have been acknowledged as received, and authors wishing to ensure safe delivery should send a duplicate (so marked) to Washington.

Potential contributors may wish to know that the incoming flow of manuscripts for *Nature* has been so reduced by the strike that the time spent on handling and assessment is much reduced. In the physical sciences in particular, publication is now extremely rapid.

The Great Greenhouse Scare

THE belief that the civilized world will one day be washed away by the increase of sea level that might result from the melting of the Antarctic ice which in turn might be accomplished by the accumulation of carbon dioxide in the atmosphere has been for some years the popular and frightening legend much quoted by public speakers, politicians and professional doomsday men. And the tales of impending doom have often been so vivid that many innocent souls must have found it hard to look at the sea without fearing engulfment. The culprit, of course, is the burning of fossil fuel, for decades now one of the raw materials of industrial society, so that the threat posed by the presence of carbon dioxide in the atmosphere has been for many people yet another stick with which to beat technology. In the circumstances, it is valuable that the MIT Press has now published the report of a study group which met at Williams, Massachusetts, last summer under the title of the 1970 Study of Critical Environmental Problems. Among other things, this careful study shows that the greenhouse effect, as it is called, has been a greatly exaggerated topic for anxiety.

There seems to be no doubt that the concentration of carbon dioxide in the atmosphere is increasing steadily—measurements at several sites suggest that in the past decade carbon dioxide concentration has increased by 0.2 per cent a year to about 320 parts per million. The amount of carbon dioxide released each year into the atmosphere is a simple function of the amount of fossil fuel burned, at present rather more than 10^{10} tonnes a year. The atmospheric reservoir of carbon dioxide appears to be about 2.5×10^{12} tonnes, so that the annual increment of carbon dioxide to the atmosphere is a substantial fraction of one per cent.

One interesting question is to know what happens to this carbon dioxide. The atmosphere is linked with two other reservoirs of carbon—the biosphere and the upper layers of the oceans. The authors of the report guess that the stock of carbon in the biosphere is comparable in size with that in the atmosphere but probably larger, and that the effective size of the oceanic reservoir depends crucially on the time scale considered to be relevant—the carbon in the first 100 metres or so of sea with which atmospheric change is comparatively rapid should be between a fifth and a half of the atmospheric reservoir, but the first kilometre would include a very much larger amount of carbon dioxide.

In these circumstances, it is not surprising that roughly half of the annual addition of carbon dioxide to the atmosphere disappears. In an entirely natural world, no doubt, one consequence of adding carbon dioxide to the atmosphere by the exhausts from fossil fuel chimneys would be to increase the growth of plant life. This, in practice, is now a matter on which agriculturists have as much to say as the persistent burners of fossil fuel, and one valuable service provided by the Williams study is that it shows how pronounced changes in the pattern of agriculture—the removal of the great tropical forests, for example—could have as marked an effect on the atmospheric reservoir of carbon dioxide as the past decade's consumption of fossil fuel. For both reservoirs, however, it is now clear that the processes of exchange between the atmosphere and the other reservoirs are at least sufficiently rapid to ensure that additions to the atmosphere are not permanent, which means that if the worst came to the worst and there were signs that carbon dioxide concentrations in the atmosphere were becoming large enough to bring about a change of temperature comparable with the natural fluctuation from one decade to another, it would be feasible to undo the damage simply by calling a halt to the rate at which fossil fuels are consumed.

What of the effects of carbon dioxide once in the atmosphere? What emerges most clearly from the study group's report is that the predictions of the simple greenhouse effect are an upper limit. With reasonable assumptions about the continued consumption of fossil fuel, the study group suggests that there may be an increase of 18 per cent in the concentration of atmospheric carbon dioxide by the year 2000, and the simple consequence of this in an entirely static atmosphere would be to increase the temperature of the surface of the Earth by about 0.5 degrees and to decrease the temperature of the stratosphere above 20 kilometres by about one degree. The snag here is that these calculations leave entirely out of account the way in which increased heat energy near the surface of the Earth would tend quickly to be dissipated by meteorological processes of various kinds. At the very least, there would be increased evaporation and, at the same time, increased absorption of carbon dioxide by the oceans. But quite a lot of energy would also be carried higher into the atmosphere by cyclonic processes. In short, half a degree by the end of the century (by which time nuclear power should have taken the load off the fossil fuels) is much more than sober men should worry about.

Who would Live in California?

THE most remarkable feature of last week's earthquake in California (see page 520) is that an event which rates merely 6.5 on the Richter scale, and which causes fewer than a hundred people to die, should attract such attention. After all, the Los Angeles earthquake is not the first serious event of its kind to have occurred this year. On this occasion, the Italians have a doubtful pride of place with an earthquake just north of Rome. And the past few years have seen much more spectacular and damaging events in Iran, Turkey, North Africa, Jugoslavia, the Philippines and Chile. On the average, earthquakes such as that in Los Angeles last week occur about a hundred times a year in various places in the world. The records show that on the average there should be about twenty earthquakes of magnitude 7.0 or greater in a year. In these circumstances, the only explanation for the interest which the Californian earthquake has excited is that it has occurred in one of the few nations in which communications of all kinds are so good that the disaster can be described almost as it happens, not merely when rescue teams have been able to thread their way over broken ground days afterwards. But an earthquake in California is also remarkable because it is a reminder that those who live there do so in the knowledge that earthquakes are a part of Californian life. Is it courage or foolhardiness that makes people live there in ever-increasing numbers?

By now, the properties of the San Andreas fault system are quite well described. Measurements in the past decade have shown that on those sections of the fault where movement is comparatively uninhibited, the annual displacement may be as much as three centimetres a year. Where the fault runs out to sea, in the southern suburbs of San Francisco, however, the fault appears to be locked as it is in the more complicated region to the south, around Los Angeles. But it has also become clear in the past two years or so that the scale of the tectonic movements responsible for the movement along the San Andreas fault is so great that the movement is bound to be as persistent as any geological process. Briefly, two tectonic plates are moving relative to each other and the fault system in California is merely a consequence of that. If anything, the development of plate tectonics should have sharpened the anxieties of those in California who fear that it can be only a matter of time before there is a much larger disaster than last week's comparatively small earthquake caused.

The first thing to be said is that the system of faults in California is so complicated, and the coastal strip is for much of its length so narrow, that there is very little hope of avoiding trouble by siting buildings away from the immediate locality of known faults. In any case, the damaging effects of a large earthquake reach several miles out from the source of trouble. It is true that mountain sites are probably safer than those in valleys or on the flat, but the extent to which a building will be shaken by a serious disturbance probably depends much more on a detailed relationship of the foundations of a building and their substratum than on any simple rule of thumb. According to Dr Charles Richter, there have been three earthquakes in California of magnitude greater than eight in the past century, one of them the San Francisco earthquake of 1906. Earthquakes of magnitude greater than seven are more frequent, perhaps four a century, but earthquakes of magnitude six, which are quite large enough to cause great damage in a city which is sufficiently near by, occur in California on an average once a year. Evidently there are few places reasonably close to the fault system at which the risk of earthquake damage can be considered small. In fifty years, four of the magnitude six earthquakes have occurred in circumstances as damaging as that last week, a frequency of roughly eight per cent. Would it therefore be reasonable to suppose that there will be a repetition of last week's trouble every twelve years on the average, an earthquake of magnitude seven near some important town every century or so and an earthquake of magnitude eight damaging a region up to a hundred miles across every two centuries or so? Or would it be prudent to suppose that the pattern of the past, with damaging earthquakes in southern California (1857) and San Francisco (1906) will be repeated at some point in the years ahead? These are questions for gamblers to attempt to answer. Whatever the truth, and given the way in which the continuing development of California implies that each year the risk that an earthquake will be near an important centre is increased as is the density with which dollars are invested in bricks and mortar, the average anticipated cost of earthquakes in California must amount to several hundred million dollars a year, the equivalent of a tax of, say, $25 per head per year for California as a whole.

Merely to make this kind of calculation, full of speculation as it is, is a powerful reminder of the scale on which California should be planning for its uncertain future. Although there may yet be developed means of warning people of immediately impending trouble, there is no chance that earthquake prediction will ever be married to regional planning with such delicacy that people will know where not to build towns and factories. The best that can be hoped for is advice for evacuating them in time. It is also improbable that some of the techniques being talked of for relieving pent-up stresses in association with fault systems will be able, if ever successful, to avert any but the obvious dangers. In the circumstances, what California needs most urgently is not so much research on earthquake mechanisms, important though that may be, but a well-run state-wide insurance programme which will allow the frontiersmen of California to pay for the cost of earthquake disasters year by year, not only when disaster strikes. There is no reason why those living in California now should evacuate it, but is there not a case for thinking that those about to move there to build factories should think of going elsewhere?

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100 Years Ago

THE MICROSCOPE

IMPROVEMENTS IN THE LENSES OF MICROSCOPES

FOR some time, people in England have been content to let the improvement of the optical powers of the microscope remain entirely in the hands of the makers, believing, apparently, that Mr. Lister had effected all in his suggestions and improvements that could be desired. Dr. Royston Pigott, an able mathematician, formerly Fellow of St. Peter's College, Cambridge, and a Doctor of Medicine of that University, was not, however, inclined to look at the matter in this way, and for many years has been working and experimenting with a view, first, to test the accuracy of our best object-glasses, and, secondly, to suggest means for their improvement. It should be remembered that Oberhauser, Nachet, and especially Hartnack, on the Continent, not satisfied with the old system of combinations for object-glasses, and not having the benefit of Lister's researches, have made excellent objectives on a totally different system, and during the last few years the last-named maker has carried his system of "immersion lenses" to such a point of excellence as really to surpass the best glasses on Lister's system, in definition, penetration, working distance, and illumination. Those who do not admit the excellence of these objectives, which are now used by nearly all German histologists, have probably seen older glasses, made at a time when Hartnack had not reached his best. It is worth stating, now that the Parisian opticians are inaccessible, that Gundlach of Berlin has succeeded in making excellent glasses of high power at astonishingly small prices, some of his 1-12ths and 1-16ths immersion 1-16ths (so-called), being admirable in their performance. They are not, however, equal to Hartnack's glasses, which, though costing far less than what similar English glasses cost, yet are more expensive than Gundlach's. It is only fair to all parties concerned to state that the terms 1-8th, 1-12th, 1-16th, &c., as now applied to an object-glass, appear to have no definite meaning, but depend on the caprice of the maker, since the magnifying power of glasses, with the same fraction assigned to them, differs enormously.

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OLD WORLD

COMPUTERS

More Favours for ICL?

In its year-old examination of the British computer industry, bisected by the general election, the House of Commons Select Committee on Science and Technology is once again taking evidence from government departments. Judging by last week's session with representatives of the Department of Trade and Industry, much of the evidence taken before the election should still be relevant. According to Dr I. Maddock, Controller of Industrial Technology in the department, there has been no significant reorganization of the divisions of the department that deal with computers and electronics, no significant change in their staffing, and no change in the relationship of the department with the Ministry of Defence, the Atomic Energy Authority, and the Civil Service Department. But a review is under way of the manner in which computers are bought for government departments, and a ministerial announcement is "not many weeks away".

Much of the discussion revolved around the amount of research and development that the British computer industry needs to do in order to sustain itself, a theme which the committee continually returned to last year. Dr Maddock reckoned that an expenditure of £15–20 million for several years would be needed to bring a family of computers into the market place, but Mr Ian Lloyd, a member of the subcommittee, thought this a serious underestimate bearing in mind that the 360 series cost IBM $3–4 thousand million. Dr Maddock's reply was that this sum included leasing finance, software and so on, and that £1 buys more R & D work in Britain than does $2.4 in the United States.

Including payments to ICL under the merger agreement, the total amount of R & D work sponsored by the government through the Department of Trade and Industry was £17 million last year and £16.1 million this year. During the period 1964/65 to 1969/70, SRC research grants in the same area came to £2.8 million. It is difficult to say how much the British computer industry itself is spending on R & D, chiefly because a large part of it is American-owned and to some extent living off research in the United States and because the industry also benefits from research in electronics, but Dr Maddock put last year's expenditure at £20–25 million. The new government has agreed to fulfil its obligations under the merger agreement with ICL, but there has been no discussion about future payments after the last payment under the agreement of £2,250,000 which is due in April.

It was clear that Dr Maddock would like to see the government give greater preference to British computers in its purchases, although he pointed out that it is frequently difficult in this context to say what is "British" and what is not. Sometimes it is necessary to examine individually each model that a firm produces to discover the extent to which it contains British components, and in central government a computer is defined as British if fifty per cent by value is British. Dr Maddock's personal opinion was that there should be what he called a "Buy British Act" along the lines of the "Buy American Act" which operates in the US Department of Defense and has given a boost to American producers. Indigenous software should also be preferentially treated, in so far as this could be done.

Towards the end of the session the committee steered the questioning toward the problems of the National Computing Centre, which was examined the previous week (*Nature*, **229**, 444; 1971). Dr Maddock talked of a change of tempo in the affairs of the centre; the department is speeding up the rate at which the centre is moving towards self-support. One of Dr Maddock's colleagues, Mr J. W. Nicholls, said this desire of the department was reflected in the reduction in the grant-in-aid which the centre will receive next year. But Dr John Cunningham, a member of the committee, referred to the view in the computer industry that the National Computing Centre should restrict itself to non-profit-making activities, and wondered how this could be reconciled with the department's aims for the centre. Mr Nicholls thought that ways could be found for funding specific projects that were in the national interest, and that the centre could earn money by giving advice to foreign governments. As a member of the council of the centre, Mr Nicholls said that he intends to see it slimmed down, but he was in favour of keeping the centre and of pushing it towards Europe.

POPULATION

Gloom in the Lords

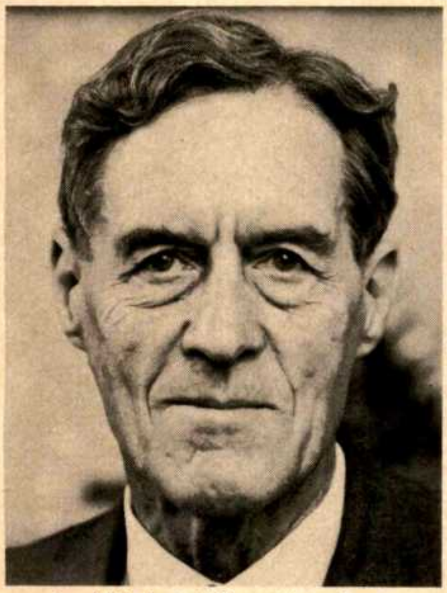
Gloom, mixed with occasional optimism, filled the chamber of the House of Lords last week during a wide-ranging debate on the growth in world population. Lord Snow, who initiated the debate, said he believes that "the future is black", chiefly because mankind is too concerned with parochial problems to devote enough attention to important issues which face the world. On the side of the optimists, however, Lord Blackett confessed that he is like the would-be eighteenth century philosopher who tried to learn philosophy but gave it up, because "cheerfulness keeps breaking in".

The gloom was cast by the figures given by Lord Snow when he opened the debate. The world population had reached 1,000 million by 1830, and it increased to 2,000 million by 1930. Between 1930 and 1960, another 1,000 million people were added, and by now the world population has probably reached 3,500 million. At the end of the century, the figure will be near 7,000 million and, according to Lord Snow, unless action is soon taken, there will be 14,000 million people on the Earth early in the next century. "These are terrifying figures," Lord Snow said, and he laid much of the blame for the situation at the door of medical technology. This technology, he suggested, had spread throughout the world faster than any other so that infantile mortality in any part of the world—poor or rich—was greatly reduced. "Technology, remember, is a queer thing," he said; "it brings you gifts with one hand and it stabs you in the back with the other."

But the answer, of course, is not to restrain medical technology, but to get to grips with the consequences. Unfortunately, however, Lord Snow had few suggestions to offer—"all the steps that one can suggest seem quite minor judged by the cataclysmic size of the whole position, the whole developing crisis". The notion that the problem of feeding such a huge population will be overcome by human ingenuity is false optimism gone mad, Lord Snow said, but nevertheless he had much to say in favour of the so-called "green revolution" and would like to see an infrastructure developed to keep the advances in crop control made in the past decade going. This meant putting more money into the activities of the World Bank and the agencies of the United Nations.

But what the problem really boiled down to is the Matthew effect—to them that hath shall be given—and Lord Snow suggested that the gap between rich and poor nations will widen unless the poorer countries can be persuaded to work from within to reduce their own rate of growth. Lord Snow's pessimism springs chiefly from the fact that he can see no real way that this can be done, and the only ray of hope that he offered is that young people are "extremely sensitive to the problem".

Society, said Lord Blackett, had thirty years in which to change its fundamental assumptions about population, and he was much less pessimistic about the prospects. "I have an irrational hunch that we are not going to destroy ourselves over this issue," he said, and he obviously took some heart from the experience of Jugoslavia, Hungary and Japan, all of which have got their birthrates down to a stable level. Lord Blackett was sure that the world could easily accommodate 7,000 million people—indeed, he could see no way in which the predicted increase during the next 30 years could be curtailed—and population policies should be aimed at securing a stable population by about half way through the next century. As a start to achieving a stable population in the world, Lord Blackett suggested that Britain should seriously consider the consequences of adopting a population policy.



Lord Blackett: "Cheerfulness keeps breaking in."

Other speakers in the debate also toyed with the idea of instituting a population policy in Britain, and this has also occupied the Select Committee on Science and Technology during the past session. But the chief problem still remains how to influence the population of the developing countries. As Lord Blackett suggested, much more thought and research into the problem are needed, but in the meantime an announcement by Baroness Tweedsmuir of Belhelvie that the government is increasing its contribution to overseas aid, to the IPPF and other agencies concerned with population studies, is welcome news indeed.

TECHNOLOGICAL FORECASTING

What Went Wrong?

THE financial flounderings of Rolls-Royce and the huge cost escalations of the Concorde project are the product of essentially the same shortcoming—a grave underestimate of the costs of new technology. The Social Science Research Council has therefore acted with a fine sense of timing in announcing that it is to give a grant of £75,000 to the Science Policy Research Unit of the University of Sussex for research into forecasting techniques. The research will be essentially a series of case studies of technological projects which have greatly exceeded their cost forecasts.

The research group involved in the study will be a mixture of social scientists and natural scientists, and the ultimate goal will be to produce a forecasting tool which eliminates the almost inevitable bias towards underestimating costs that is evident in much technological forecasting. The first step will be to determine what has caused this underestimation, and this will involve separating the deliberate bias from the accidental bias. The SSRC believes, for example, that underestimation of costs may be due in part to "a fundamental conflict of interest between scientists and engineers on the one hand, and managers and accountants on the other"—engineers may deliberately underestimate the difficulties in order to get a project accepted by the board of directors.

Having separated the deliberate from the accidental bias, the Science Policy Research Unit intends to use the findings to develop a technique for technology assessment which also includes provision for social effects of new technology. This involves an analysis of the effect on social attitudes of the failure of technology to live up to the promises that are made on its behalf by the forecasters.

CHEMICALS

BP in Trouble too

INFLATION seems to be overtaking the chemical companies one by one. Less than a month ago Shell Chemicals announced a "reappraisal" of its huge expansion at Carrington and Stanlow (see *Nature*, **229**, 291; 1971) and now BP Chemicals International has announced the cancellation of a benzene project at Grangemouth which was to have cost more than £1 million, and the rephasing of the construction of a chemical plant at Baglan Bay, South Wales.

Most of the plans for the Baglan Bay project were completed at the end of 1968 but the total cost has now escalated by about 20 per cent to £100 million. It seems, however, that only one or two of the later plants within the complex will be affected. BP Chemicals is planning a purge on operating costs to try to combat the effects of inflation and the inevitable targets are the wages and salaries bill, and research and development. The company believes, however, that it will be able to streamline its research and development effort so that it will cost less but produce the same results.

At the end of last year, the parent company, British Petroleum, was obliged to arrange short term credit amounting to about £100 million because of difficulties in the tanker charter market; this fact and the last set of quarterly results only serve to emphasize the difficult period which BP and the rest of the chemical industry are going through.

CANCER RESEARCH

ICRF Expands

THE Imperial Cancer Research Fund (ICRF) last week announced the establishment of two more research units, a medical oncology unit which will be accommodated at St Bartholomew's Hospital, and a tumour immunology unit, eventually to be housed in new buildings at University College, London. It seems likely that research in the new units will begin in October this year.

The establishment of these extramural units is a clear departure from the Fund's previous research policy; in the past, the ICRF has supported research into cancer chiefly through work carried out in the Fund's own laboratories at Lincoln's Inn Fields and at Mill Hill. As the demand for space at these sites has intensified, however, it has become necessary to find other ways of housing specialized and important research projects. The first indication of this fresh approach was the establishment of the breast cancer research unit at the New Cross Hospital in 1969. The new units, however, are evidence not only of expansion in terms of space, but also in terms of cooperative research.

St Bartholomew's Hospital will provide accommodation and hospital facilities for the medical oncology unit, but the ICRF will pay the running costs, which have been estimated at £250,000 over five years. An important feature of this unit will be the connexion which can be established through the director, Dr G. Hamilton Fairley, between the unit and the Chester Beatty Research Institute, where Dr Hamilton Fairley will continue his research on a part-time basis. The eventual scheme is for links to be forged between the ICRF, the Chester Beatty, St Bartholomew's Hospital and a large regional hospital. Such cooperation should lead to unique opportunities for clinical cancer research. Dr Hamilton Fairley regards the unit as the clinical arm of the ICRF; he is particularly anxious that the plan should make it possible for cancer patients to be treated at the unit before they have received any other treatment which could complicate their symptoms.

The ICRF is providing about £82,000 to cover the cost of building and fitting out the tumour immunology unit at University College, and a further £300,000 will be found over five years to pay the running costs. The total financial commitment for the first five years that the two units will be in existence is therefore just over £0.5 millions. Finance will be provided chiefly from the ICRF's annual income, but there is a substantial reserve fund available to cover inflation.

The tumour immunology unit will be run by Professor N. A. Mitchison, and recruitment of research staff has already begun.

NUCLEAR POWER

Rethinking at BNDC

THE Nuclear Power Group, one of the two consortia set up during the reorganization of the British nuclear power industry in the late 1960s, seems to be losing the competition of its twin, British Nuclear Design and Construction Ltd, in the field of steam generating heavy water reactors (SGHWR).

Although BNDC says that development work on the SGHWR will be continued, it certainly seems that the consortium's prices are not as competitive as those of the Nuclear Power Group. The NPG is, for example, very hopeful of winning the contract for the Jervis Bay project in Australia whereas the BNDC tender was not even shortlisted. Another clue to the changing attitude of BNDC towards the steam generating reactor is the consortium's decision not to compete for the Stakeness reactor contract offered by the North of Scotland Hydroelectric Board. The NPG, however, regards the Stakeness contract as vitally important because it marks the first expression of real commercial interest in the SGHWRs within the UK.

The Nuclear Power Group is also confident that the SGHWR is a particularly good export proposition because it does not require the large and sophisticated high pressure boilers which are necessary in pressurized water and boiling water reactors. The group says that as much as 85 per cent of a typical SGHWR can be constructed within the purchasing country, even if that country is not particularly advanced technologically. The design of steam generating reactors is also very flexible and higher outputs can be achieved simply by adding extra light-water tubes rather than by carrying out fundamental boiler design changes.

The decline of SGHWR impetus within BNDC may also reflect some rethinking within the GEC–English Electric–AEI group which owns 25 per cent of the consortium. The GEC group is known to be pursuing an internal policy of reducing the number of designs across its whole range of power engineering products in an effort to reduce costs and increase reliability. It is also significant that the GEC group is taking an active interest in a Westinghouse design for a pressurized water reactor and is involved with Westinghouse in a £60 million contract for such a reactor in South Korea.

Miscellaneous Intelligence

OPPONENTS of supersonic flight have been slow to point out that the bankruptcy of Rolls-Royce Limited has cast yet another cloud on the Concorde project. Theoretically, at least, the official receiver now in residence at Derby may eventually decide to close down the Bristol Division, the company at present manufacturing Olympus engines, in which case supersonic flight would presumably be delayed for several years. To be sure, a much more likely course of events is that Sud-Aviation would put in an attractive bid for the Bristol Division. Presumably with the interests of shareholders in mind, the receiver in bankruptcy would be compelled to sell, thus helping to ensure that what began as a collaborative aircraft finishes up almost entirely made in France.

THE visit of Mr Andrew Stein, State Representative in the New York State Assembly, seems to have replaced the Federal Aviation Board as the target of those xenophobes in Britain who believe that the United States seeks to hamper British innovation in aircraft by applying footling regulations. Resentment has still not entirely disappeared over the row fifteen years ago when the British aircraft called Britannia, named Whispering Giant by its advertising agents, was denied a certificate until its landing gear was modified. Mr Stein's apparently innocent bill to limit noise at New York airports to 108 perceived noise decibels by July and by 98 p.n.d. by 1977 could be such a serious threat to the viability of Concorde that Mr Anthony Wedgwood Benn, once Minister of Technology but still MP for the Bristol constituency in which Concorde is manufactured, is off to New York next week to put the opposing case. But if Mr Stein should get his way, there may still be time to reconsider the best arrangement yet for using supersonic transports—a shuttle service between Newfoundland or Maine and Ireland, with subsonic feeder services from the terminals.

ONE SIGN that may be taken as proof that the polytechnics will in due course be just like other universities is that the students at the North London Polytechnic, an amalgamation of the Northwestern Polytechnic and the Northern Polytechnic in London, have been protesting against the appointment of Professor T. G. Miller as principal on the grounds that Professor Miller was for two years principal of the University College of Rhodesia. What the polytechnic needs now to establish its claim to be taken seriously as an establishment of higher education is, first of all, a visit from Mr Enoch Powell (whose car can be stopped by shouting crowds) and an opportunity to say no to a speaking engagement by the recent Prime Minister, Mr Harold Wilson, or the present Home Secretary, Mr Reginald Maudling.

Parliament in Britain

Swann Report

MR JAMES PRIOR, Minister of Agriculture, said that the government intends soon to implement many of the recommendations contained in the Swann Report on the use of antibiotics in medicine. The retail sale of feeding stuffs containing certain antibiotics will be made unlawful except on prescription, to prevent antibiotic-resistant strains of bacteria being passed from animals to humans. From March 1, 1971, penicillin, chlortetracycline and oxytetracycline will be restricted, and from September 1, 1971, tylosin, sulphonamide drugs and four nitrofurans will be brought under the regulations.

Mr Prior also announced that some drugs will be derestricted next year. (Written answers, February 11.)

Research Expenditure

THE research associations governed by the Department of Trade and Industry have been deriving a steadily growing proportion of their income from contract research during the past five years. Sir John Eden, Minister for Industry, said that the value of such work carried out by the associations in 1964 amounted to £799,516, but in 1969 it had reached £1,944,394. These totals represent 8.7 per cent and 13.5 per cent of the total gross income of all the Department of Trade and Industry in 1964 and 1969 respectively.

In reply to a later question, also from Mr John Osborn, Mrs Thatcher, Secretary of State for Education and Science, said that in 1968–69 payments for research services and other appropriations in aid contributed about £3 million—less than 10 per cent—to the expenditure by research council establishments and research expenditure by the Natural History Museum. Public corporations and private industry provided £4.1 million for research in universities. This amounts to about 4.6 per cent of the universities' expenditure on research and development in that year. (Written answers, February 8.)

CS

MISS BERNADETTE DEVLIN asked a series of questions about the toxicity of CS and use of the agent in Ulster. She asked whether the Ministry of Defence has ruled out the possibility that prolonged or repeated exposure to CS can lead to accumulation of cyanide in animal tissues, and whether there is any indication that CS can have a deleterious effect on sufferers from asthma. But Mr Ian Gilmour, Under-secretary of State, Ministry of Defence, replied that cyanide is not a cumulative poison and that there is no evidence to suggest that people suffering from asthma are unduly affected by CS. (Written answers, February 10.)

Select Committee probes Embarrassing Area

"THE past and present state of Britain's space activities . . . has been a story of wasted opportunities brought about by lack of purpose and the absence of any coherent organization. There has been no real space policy and no space programme as such." Nearly four years ago, the House of Commons Estimates Committee used these words to preface a string of recommendations for reforming the organization of space research in the UK. Few of the committee's recommendations were taken up, most were ignored and there is still no overall policy for British space research.

As a subcommittee of the Select Committee on Science and Technology has discovered from only two public hearings, the vesting of responsibility for much of British space research in the Ministry of Aviation Supply has not helped to coordinate activities. Individual ministries are still responsible for space activities which fall within their own departments' terms of reference, while the Ministry of Aviation Supply sits in the centre, looking after some of the international programme and going its own way with launcher development in the UK. Some indication of the fragmentation of British space research can be gained from the fact that last year out of a total budget of nearly £17 million for national space activities, the Department of Education and Science was responsible for £4 million, the Ministry of Defence for £6.7 million, the Ministry of Posts and Telecommunications for £1.6 million and the Ministry of Aviation Supply for £4.6 million (see *Nature*, **229**, 362; 1971). In spite of the fact that the Ministry of Aviation Supply is nominally in the centre of this activity, providing technical assistance and expertise to other departments, when the members of the subcommittee asked questions of representatives from the ministry, they were invariably told that the Ministry of Aviation Supply is not responsible for that particular aspect of research or development. The committee has therefore been unable to glean much information about how priorities are established in planning space research, and there is even a hint of suspicion in the evidence taken so far that such priorities cannot be formulated under the present arrangements.

As far as international cooperation is concerned, Mr Palmer's subcommittee will discover that the British government's attitude has been less than consistent during the past decade. To be sure, this inconsistency is a reflexion of the muddle into which the European organizations have got themselves, but again there have been difficulties because responsibility for all aspects of international cooperation in space research is vested in several different departments. The Ministry of Aviation Supply is responsible for British participation in ELDO, the Ministry of Posts and Telecommunications for INTELSAT and other post office studies, and the Science Research Council sends delegates to ESRO and negotiates with NASA for the launching of British scientific satellites.

On launcher development, however, a clear policy has emerged during the past few years—the government will not participate in European launcher development if it means duplicating research and development that has already been carried out in the United States. This policy has led to almost complete British withdrawal from ELDO, and is chiefly responsible for the present state of limbo about participation in the post-Apollo programme. While there was an opportunity of using the Blue Streak launcher as the first stage of a small European launcher, the British government enthusiastically supported ELDO, but when the organization decided to go ahead with development of a much larger launcher, Europa 3, the government decided to limit the British contribution to ELDO to £11 million from January 1, 1969. About £10 million of that money has now been spent.

The chief argument behind this policy is that while Europe can buy launchers from the United States, it is wasteful, both in terms of money and resources, to develop an independent European capability. A much better area in which to invest is applications satellites, and the government's policies towards ESRO and in the European Space Conference have been geared towards this end. But this concentration on applications satellites has, in many ways, created more difficulties for organization in Britain—although the SRC is responsible for sending delegates to the ESRO council meetings, the UK contribution to the cost of studies on applications satellites is taken from the Ministry of Aviation Supply's budget. So once again there is split responsibility, and the situation is even more confused by the fact that part of the studies on ESRO applications satellites is concerned with a communications satellite, and this area is usually the responsibility of the Ministry of Posts and Telecommunications.

Although there is plenty for Mr Palmer's subcommittee to get its teeth into when it investigates Britain's international space policies, it is on the domestic front that the subcommittee is likely to discover the most to criticize. The UK's national space programme falls essentially into three parts, each of which is the responsibility of a separate ministry. The Department of Education and Science has been involved in the development of the highly successful Skylark sounding rocket, 202 launches of which have been made since 1957, and the DES is also responsible for development of a series of scientific satellites in cooperation with the United States. Three of these satellites have now been successfully launched, a fourth is due to be launched later this year, and a fifth in 1973. A defence communications satellite has been developed by the Ministry of Defence, and was launched by the US in 1969. Finally, the Ministry of Aviation Supply is responsible for the development of the Black Arrow Launcher and a series of technological satellites which Black Arrow should place in orbit during the 1970s.

The subcommittee has already asked a few embarrassing questions of the representatives from the Ministry of Aviation Supply about development of the Black Arrow launcher, and it seems that its rather mediocre performance so far is causing some consternation in the committee. Black Arrow is a small rocket, designed to place a payload of 120 kg into a near-Earth orbit. So far, of the three development firings, one has been a success, one failed in the guidance control, and the other failed in the second stage pressurization. Nevertheless, the Ministry of Aviation Supply is going ahead with another launch attempt in the autumn, and the subcommittee was told that a further series of satellites for testing components and subsystems "for use in future satellites" has been suggested for the 1970s. Development of the Black Arrow, it seems, has turned out to be much more expensive than the ministry first envisaged, and the whole programme is due for review later this year.

Mr Palmer's subcommittee will evidently want to satisfy itself that the Black Arrow project is giving value for money, and that the experiments planned for future satellites will provide results that are likely to be useful to other departments. This, of course, implies that British space activities should be much more closely integrated, and that some attempt should be made to coordinate the activities of the various departments. As the Estimates Committee said in 1967, "many departments and many committees have spent much time looking at aspects of space, but it has never been considered as a whole".

NEW WORLD

Earthquakes trigger Reports but no Funds

by our Washington Correspondent

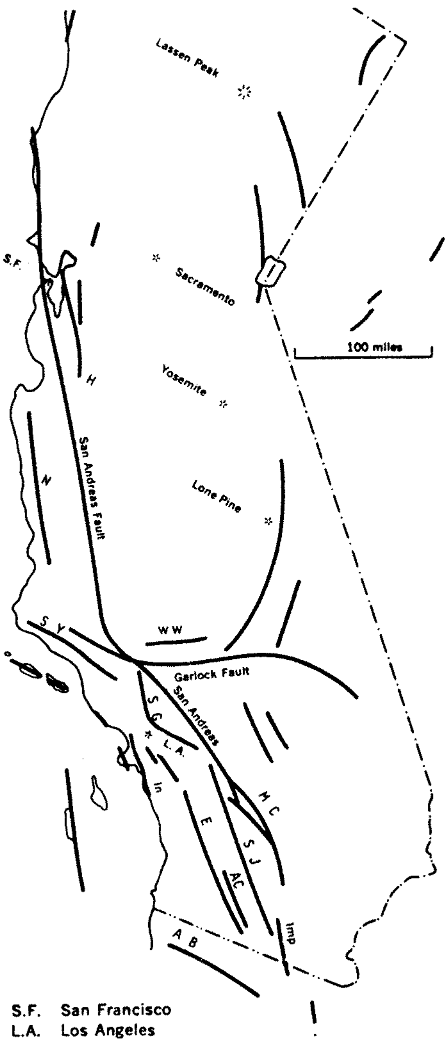
"IMMEDIATELY following a destructive earthquake the public is aroused and, in response, public officials are attentive to the problem. Demands are made for more and better earthquake protection, but memory of the event quickly fades; in a few years, as long as there is no disastrous event, the public feels that everything is under control, and public officials turn their attention to problems seemingly more urgent." Thus a report published in 1969, accurately prophesied the reaction to its recommendations. At least six reports on earthquakes have appeared since the Alaska earthquake of 1964, two apiece from the Office of Science and Technology and the National Academy of Sciences, one from the National Academy of Engineering and one from the Federal Council for Science and Technology.

Each report has arrived at broadly the same list of recommendations. The reports differ only in the amounts of additional research funds that they ask should be made available. As methods of predicting and controlling earthquakes grow less distant, the number of seemingly worthwhile research programmes increases accordingly, so that the requisite investment in earthquake research has escalated from about $26 million a year recommended by a report in 1965, to more than $60 million a year by 1969. Government spending has in fact grown from about $5 million a year in 1965 to $8 million this year.

It is too early to tell whether the earthquake that shook South California last week will be any more effective than was the Alaska earthquake at opening the doors of treasury vaults. In terms of casualties—probably the crucial factor in securing action—both events have been as sparing of human life as they have been destructive of property. Only 115 people died in the Alaska earthquake—a festival on the pier and waterfront of Seward, wholly wiped out by the earthquake, was cancelled at the last minute—and so far the toll in last week's tragedy is less than 70. But despite the small size of the southern California earthquake, which registered only 6.4 on the Richter scale, damage to property is estimated at about $1,000 million, It is also disturbing that several of the structures destroyed, including bridges and buildings, were designed to be resistant to earthquakes.

The San Andreas fault, which strikes through California on a north-west-south-east axis, has caused two major earthquakes in the past 120 years, one in Los Angeles in 1857 and the San Francisco quake of 1906. Since these events seem to occur once in every 60 to 100 years, another major earthquake—7.75 or higher on the Richter scale—can reasonably be expected at any moment.

Unlike the great majority of earthquakes, which come and go with nobody any the wiser, the southern California earthquake is being fairly well documented. Some 20 portable instruments of the Geological Survey and Coast and Geodetic Survey have now been moved to the site to record aftershocks, although at the nearby seismic observatory at Pasadena many of the instruments went off their scales during the main shock.



S.F. San Francisco
L.A. Los Angeles

FAULTS LETTERED AS FOLLOWS:

H	Haywards	AC	Agua Callente
N	Nacimiento	Imp	Imperial
WW	White Wolf	AB	Agua Blanca
In	Inglewood	SY	Santa Ynez
E	Elsinore	MC	Mission Creek
SJ	San Jacinto	SG	San Gabriel

An intensive study of the earthquake is also being planned by the National Science Foundation. Like other agencies with an interest in earthquake studies, however, the foundation's means are insufficient for its needs. A programme of earthquake engineering research, initiated in 1965 in response to the Alaska earthquake, now disposes of $2 million a year, increased to $3 million in the budget for 1972, and a total of $1.5 million is spent on geophysical research related to earthquakes, mostly seismology, laboratory studies of rock behaviour and surveys of the variations in magnetic field across the San Andreas Fault. Other agencies conducting earthquake research include the Geological Survey, which spends about $1.5 million a year, much of it in support of the National Centre for Earthquake Research in Menlo Park, California, the Atomic Energy Commission and the Coast and Geodetic Survey. There is no coordinated research programme of the type envisaged by a succession of recent reports.

A panel chaired by Professor Frank Press of MIT, for example, prepared a report for the Office of Science and Technology in 1965 entitled *Earthquake Prediction: A Proposal for a Ten-Year Program of Research*. This contained suggestions for studying earthquake generation and prediction, including the installation of a network of seismometers in California and Alaska. The programme should be supported at the level of $268 million over ten years, of which $60 million was earmarked for earthquake engineering. The chief result of the report was to initiate two further reports, one of them commissioned by the Federal Council for Science and Technology and the other by the National Academy of Engineering. The council's report, *Proposal for a Ten-Year National Earthquake Hazards Program*, was written by an interagency panel under the chairmanship of Dr William T. Pecora, director of the Geological Survey, and completed in 1968. It recommended a programme essentially identical with that put forward by the Press panel, though with a heavier emphasis on fire hazards and the socio-economic problems associated with earthquakes, and called for a ten year budget of $218 million, exclusive of engineering research.

The National Academy of Engineering, for its part, produced in 1969 a report devoted to the engineering aspects of earthquakes, *Earthquake Engineering Research*, which proposed the expenditure of $38 million a year over a ten year period for those aspects alone. The report, produced by a committee chaired by Dr George W. Housner, of CalTech, urged the setting up of a panel to coordinate research carried out by the various government agencies and universities, and suggested that the National Science Foundation should assume the lead in directing the research effort.

1969 was a good year for reports about earthquakes and two more were to erupt before the year was out. *Toward Reduction of Losses from Earthquakes*, issued by the committee on the Alaska earthquake of the National Academy of Sciences, presented in summary form the main recommendations deduced from study of the 1964 earthquake. These included the call for more research into the development of earthquake resistant structures, earthquake forecasting and loss reduction, as well as for improved arrangements for gathering seismic data. A second report, produced by the committee on seismology of the National Academy of Sciences, repeated the plea for a national ten-year effort in seismology, the major part of which, it says, should be devoted to research on earthquake hazards and earthquake prediction and control (*Seismology: Responsibilities and Requirements of a Growing Science*). The committee envisaged that federal support of seismology, then running at about $10 million a year, should increase to $35 million by fiscal year 1971, and then to £50 million and above, making a round total of $500 million over the decade of the 1970s. Earthquake-related items in this imagined budget included $175 million to be devoted to prediction and prevention of earthquakes (exclusive of engineering), $55 million for instrumentation and observation and some $40 million for studying the physics of earthquake processes, making a total of some $270 million.

The chief difference between NAS and NAE reports of 1969 and the OST report of 1965 was that the latter proposed a ten year budget of $218 million for geophysical and other research, and $60 million for engineering research, while the former reports proposed sums of $270 million and $380 million respectively for these two categories of research. Perhaps because all these reports had only a token effect on federal expenditures, the most recent government effort in this direction avoids all mention of money and merely repeats the same list of recommendations.

Earthquake Hazard Reduction, issued last September by the Office of Science and Technology, is the report of a task force chaired by Karl V. Steinbrugge. The report counts earthquake prediction and control as benefits likely to accrue after a ten year research programme: projects likely to reap immediate reward include requiring all federal buildings to be of earthquake resistant design and preparing better seismicity maps. Applied research on earthquake engineering is deemed likely to yield fruits 5 to 10 years after commencement. The OST invited federal agencies to submit their comments on the Steinbrugge report, which were due in last month, but has taken no further action.

All six government reports prepared in the last six years have had less tangible effect than the utterances of the young clairvoyante, who predicted in 1968 that a catastrophic earthquake the following April would cause California to slip into the ocean; she at least produced a sharp increase in the airline reservations for flights out of California in March. It remains to be seen whether last week's earthquake will give any greater credence to the warnings of seismologists. But one thing seems certain: another report will be called for.

SEISMOLOGY

California Quakes Again

by our Geophysics Correspondent

The most recent seismicity maps of the Earth show the San Andreas fault and its parallel neighbours as remarkably patchy features. For the most famous and most studied fault system in the world does not reveal itself by a regular chain of earthquakes along its thousand kilometre length, but by some regions of high seismicity interspersed with others of little or no activity. Future prospects in these quiet zones are obviously a very important matter and the evidence so far

Latest Lunar Seismology

Latest reports are that the Apollo 14 seismometers are performing well and revealing very similar phenomena to those recorded by the Apollo 12 seismic package. The latter is still operating satisfactorily over a year after its installation (and beyond its nominal lifetime) and recorded the impact of the Saturn IVB rocket on the Moon. Again the extraordinary seismic records were seen with discernible compressional and shear waves and then the build-up and long ringing decay in energy over a space of two or three hours. The LEM impact was aimed between the two instruments and fills in two further points on a lunar travel time curve which is now quite well populated with impacts from LEMs and rockets. Starting from laboratory determinations of compressional velocity as a function of pressure for collected Moon rocks, it is possible to predict a velocity–depth function for the Moon which tallies remarkably well with the inferences from travel-time data now available.

The first part of the active seismic experiment—obtaining surface seismic velocities by thumping the ground in the vicinity of the Apollo 14 seismometers also appears to have worked well and yielded very low velocities (less than 100 metres/sec) for P-waves in the first few metres. The more spectacular experiment—the firing of mortars which land at distances between the thumper range and those of the impacts—has yet to be started.

The source of the ringing is still uncertain. Recent geophysical meetings have spawned an inordinate number of (often ill-informed) explanations. The front-runner at the present, however, seems to be this. The Moon rocks are assumed to have a combination of two properties not observed together on Earth—a high Q, or low absorption of seismic energy, and a heterogeneity sufficient to scatter seismic waves strongly. The incoherent but long lasting signal is the result—akin to the long rumble of thunder scattered by inhomogeneities in the atmosphere.

Meanwhile natural seismic activity continues to be recorded by the Apollo 12 instruments, and it is hoped that the addition of the second set of triaxial instruments will help to pin down the source of this activity. There are some intriguing facets. The peak of the activity seems definitely correlated with the lunar month—a correlation never satisfactorily pinned to any Earthly seismicity. In addition the events are carbon copies of each other—the traces tally wiggle for wiggle over extended periods. This in conjunction with the incoherence between different components of the ground motion is a very strong restraint on the location of the events. Experience in similar situations on Earth with heterogeneous media and scattering has shown how extremely sensitive the seismic signal is to the location of the source. Moving the source a few metres may change the whole pattern. Are the Moon events that close to one another? At the moment, it looks like it, in which case some form of venting would be the most obvious candidate.

is hopeful in some cases, gloomy in others. It seems that parts of the fault system are undergoing a continual relieving slippage not associated with earthquakes. The rest of the quiet zones must be just accumulating strain. It is generally agreed that the Pacific Plate and the North American Plate, whose boundary is the San Andreas system, are moving in a right-handed sense at 5 cm a year relative to each other. The best evidence is that fault movements during earthquakes are unlikely to exceed a few metres, so catastrophic quakes may be expected to occur every few tens of years in quiet zones where there is no slipping.

Viewed in this simple light, the earthquake north of Los Angeles appears to fit neatly into the framework. There has been no major earthquake near Los Angeles since 1857 when there was a shock comparable with the 1906 quake in San Francisco with a rupture length of at least 200 km. There have been relatively few minor earthquakes in this region in comparison with most other parts of the San Andreas fault. So if the fault was not slipping, all the signs were that something would have to go eventually. And yet the quake does not fit into this scheme of things and there is doubt among seismologists in the region whether it has done anything at all to relieve the accumulated strain.

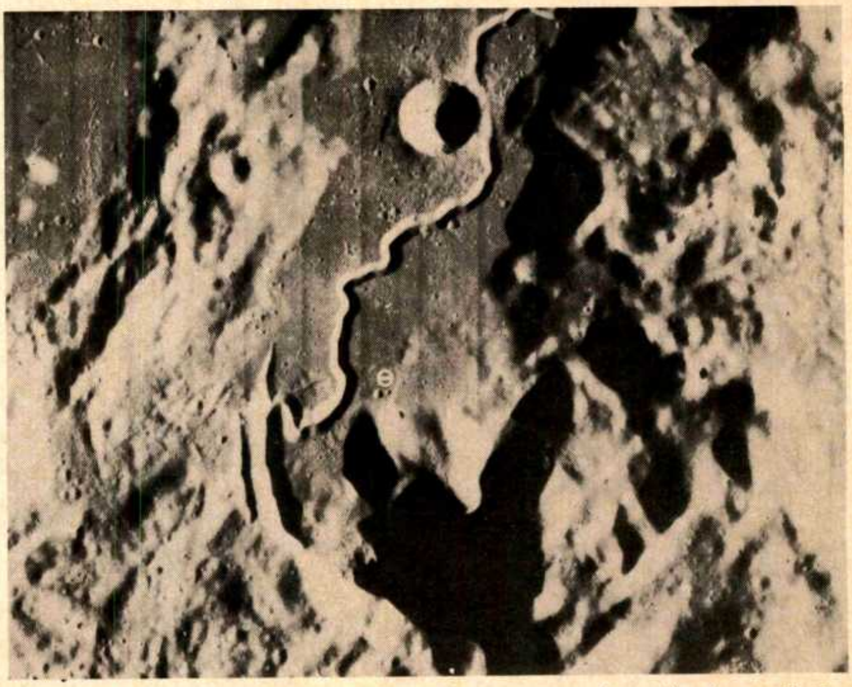
The problem is this. The best estimate so far of the location of the event is that it is 15 km north of San Fernando and 50 km north of downtown Los Angeles. Talking about a location is perhaps unrealistic for an earthquake of a magnitude of 6.5 for which the horizontal dimension of the faulting region is likely to be at least 10 km, probably much more. This whole region is completely intercepted with faults, none of which is dominant, but it can be stated with considerable confidence that the fault which moved was not the San Andreas. Nor indeed does it seem from first reports to have been the San Gabriel—a fault which runs parallel to the San Andreas. Instead it has been suggested that the ground displacements are on the Soledad Canyon Fault—a fault which appears on practically none of the maps of the area and has no known seismic history. Further, the motion does not seem to have been the right-handed strike slip associated with the San Andreas.

Much more will be known shortly when the intensive field work starts to be reported on and it will be foolish to speculate on the basis of incomplete information, but the following general points can be made. The event occurred in a region which had been relatively free of activity and seems to have a mechanism that is not immediately seen to be that of the San Andreas. This emphasizes in a dramatic way the unpredictability of seismic activity. The remarkable successes of plate tectonics are based on observations of the narrowness of most seismic belts and the consistency of earthquake mechanisms, with the idea of these belts being boundaries between moving plates. However, it is worth repeating that plate tectonics appears to be only a guide line in continental regions. Relatively new ocean crust is not intersected with pre-existing faults—continental crusts having been the object of violent forces for the past 4 billion years have much inactive faulting completely unrelated to present activity. Small wonder then that the stresses of present day movement lead to major activity away from the plate boundary as old faults take up the strain and accommodate to the latest forces. A compilation by C. R. Allen *et al.*, in the *Bulletin of the Seismological Society of America* in 1965, shows the contours of strain relief in a 30 year period to have distinctly contradictory relations to the San Andreas, and major fault movements have occurred at all angles to the San Andreas trend and at distances of up to 200 km from the main fault.

This leads to the second point—that earthquake prediction and control in a region like California require more than monitoring the major faults and (maybe) attempting to relieve strain on them. If a relatively unknown fault can suddenly break, then any reasonable effort at monitoring must be on a very broad and comprehensive basis. Fortunately there is growing interest in the work, but it is a long term project with an unclear prospect of success even in 50 years. Funding in science tends to be so oriented towards immediacy that seismologists should perhaps look to new sources—maybe more extensive support from those businesses which suffer the severest financial losses by earthquakes—insurance companies.

Thirdly, it bears repetition that there is no evidence whatsoever to associate earthquakes with unusual lunar coincidences such as the eclipse which occurred 12 hours later. Already some zealous quacks seem to have forgotten that the earthquake came before the eclipse and are claiming the effects of the eclipse were seen immediately afterwards in the quake. The Moon and Sun do indeed raise tides on the solid Earth of 30 cm but no one has yet pinned down any seismic phenomena to high tide on the Earth—and many have tried. Of course, the plane of the Moon's orbit is close to that of the ecliptic, so talk of the eclipse being an unusual strain to the Earth is idle nonsense when eclipse type conditions prevail to first order twice every lunar month.

Target for Apollo 15



With the Apollo 14 astronauts safely home, the portents are better for the next in the series, scheduled for July this year. The aim is to obtain samples from the vicinity of the Hadley Rille, and one of the landing sites which has been under consideration is marked. This time the astronauts will have the use of a roving vehicle to visit the foothills of the nearby Appenine mountains, but they will not be going into the rille itself, which is 600 feet deep. On the Orbiter photograph of the area the large crater adjacent to the rille is Hadley C, about 5.5 km across. The location of the area is at 26° 52′ N, 3° 00′ E.

NEWS AND VIEWS

Isolation of the Cholinergic Receptor Protein

It has been clear for some time that progress in the application of the techniques of molecular biology to understanding the pharmacological problems of drug receptor interaction required the ability to isolate and purify the receptor macromolecules involved. The paper by Miledi, Molinoff and Potter on page 554 of this issue of *Nature* which describes the isolation of a cholinergic receptor protein thus represents an important landmark in the development of molecular pharmacology.

The isolation of receptor macromolecules, as in any other protein purification, depends first on the availability of an abundant source material. Fortunately, nature has provided such a source in the form of the electric organ tissues of electric fishes and eels, in which there is an extremely dense cholinergic innovation of the electrical tissue and an abundance of postsynaptic cholinergic receptors which are indistinguishable in their pharmacological properties from those which exist at much lower densities at vertebrate nerve–muscle junctions. A more difficult problem has been the development of methods by which the receptor macromolecule might be identified in solubilized preparations of the membrane protein of excitable membranes. In the intact tissue the receptor can be defined operationally as 'that entity with which acetylcholine interacts to cause a change in the ionic permeability of the innovated cell membranes; such a criterion clearly cannot be applied once the receptor has been removed from the membrane. Many attempts have therefore been made to identify the cholinergic receptor by using acetylcholine or various analogues of acetylcholine on the assumption that the cholinergic receptor must possess a high affinity binding site for such molecules. Although in principle such an approach is acceptable, in practice there has been rather little success so far in the application of "cholinergic ligands" for identifying receptor macromolecules, because of the existence of many cholinergic binding sites other than the cholinergic receptor in excitable membranes, including the catalytic and allosteric sites of acetylcholinesterase. For similar reasons, there has also been only limited success in the use of reversible cholinergic antagonists, such as D-tubocurarine or atropine, as receptor labels.

This methodological impasse, however, now seems to have been overcome, and, as so often in the past, the solution lies in the application of a natural product of exotic origin and extraordinary specificity. The *deus ex machina* in this case is a snake venom toxin, α-bungarotoxin. This substance is a basic polypeptide of molecular weight 8,000 isolated from the venom of a snake from Taiwan (*Bungarus multicinctus*). α-Bungarotoxin was isolated and studied by Lee and his colleagues at the National University of Taiwan, who showed that the toxin acted as an irreversible antagonist of cholinergic receptors at vertebrate nerve–muscle junctions. They also demonstrated that this effect could be prevented by D-tubocurarine, which is a specific but reversible antagonist of neuromuscular cholinergic receptors, indication that α-bungarotoxin interacted with the cholinergic receptors.

The recent report by Changeux, Kasai and Lee (*Proc. US Nat. Acad. Sci.*, **67**, 1241; 1970) and the current paper by Miledi *et al.* in this issue describe the use of α-bungarotoxin to characterize the cholinergic receptor protein of electric organs. Changeux *et al.* found that α-bungarotoxin blocked the responses of cells in the intact electroplaques of *Electrophorus electricus* to the acetylcholine analogue carbamylcholine, and that this effect was irreversible. They also showed the same effects of bungarotoxin in an *in vitro* system, in which carbamylcholine normally increased the sodium permeability of isolated membrane fragments prepared from the electroplaques. In this preparation D-tubocurarine protected against the irreversible blocking effect of bungarotoxin, and the actions of bungarotoxin seemed to be irreversible and stoichiometric; the amount of toxin needed for complete receptor blockade was directly related to the amount of membrane material present. The actions of the toxin also seemed highly specific, because additions of membrane material prepared from the non-innovated face of the electroplaques in which cholinergic receptors are absent did not significantly decrease the antagonist effect of the toxin on innovated membrane fragments. It would seem therefore that the cholinergic receptors of the electroplaques could be titrated in a highly specific manner with bungarotoxin. The specificity of action of the toxin was also confirmed by the absence of any effect on the activity of acetylcholinesterase. Changeux *et al.* were also able to estimate the number of cholinergic receptor sites in the electroplaque tissue from the minimum amount of bungarotoxin needed to produce complete receptor blockade, and concluded that the number of receptor sites was approximately equal to the number of acetylcholinesterase catalytic sites in the tissue. Finally, Changeux *et al.* reported that bungarotoxin irreversibly inhibited the binding of radioactively labelled decamethonium in a soluble preparation of electroplaque membrane protein, suggesting that bungarotoxin could be used to identify the cholinergic receptor macromolecule in such soluble preparations.

Miledi, Molinoff and Potter have exploited the extraordinary specificity of bungarotoxin to the extent of isolating and purifying by this means what seems to be the cholinergic receptor protein. Miledi *et al.* first confirmed that α-bungarotoxin acted as an irreversible antagonist at cholinergic receptors in the electric tissue of *Torpedo marmorata*, and also at neuromuscular junctions in frog sartorius muscles. Miledi *et al.* also prepared radioactively labelled bungarotoxin of very high specific activity by iodination with ^{131}I. This material was used to study the binding of toxin to cholinergic receptor sites in a preparation of membrane fragments from disrupted electric tissue. The binding of labelled toxin was dependent on the time of incubation and the concentration of toxin, and was saturable. The rate of binding of labelled toxin was decreased in the presence of D-tubocurarine or carbamylcholine, but was unaffected by the acetylcholinesterase inhibitor physostigmine or by sodium dodecylsulphate, suggesting a specific binding of the toxins to cholinergic receptors. It proved possible to release the labelled toxin-receptor complex from the membrane fragments by treatment with a low concentration of the detergent 'Triton X-100', and the toxin-receptor complex was then purified by chromatography and density gradient centrifugation. On chromatography in the presence of detergents the toxin-receptor complex could be clearly separated from the enzyme acetylcholinesterase. The purest fractions obtained contained 1 μg of bungarotoxin per 10 mμg membrane protein, suggesting a molecular weight for the receptor protein of approximately 80,000. In the absence of detergent, the receptor protein formed aggregates of 500,000–2,000,000 molecular weight. In low concentrations of 'Triton' the receptor protein seemed to consist of a tetrameric form of the 80,000 molecular weight subunits. As in the experiments of Changeux *et al.*, the number of bungarotoxin binding sites in *Torpedo* tissue was approximately equal to the number of acetylcholinesterase catalytic sites. If the receptor protein normally exists as a tetramer, as is the case with acetylcholinesterase, this would imply that the electric tissue membrane contains equal numbers of enzymes and receptor molecules. Miledi *et al.* estimated the number of bungarotoxin binding sites as approximately $10,000/\mu^2$ of cell membranes.

Although the present reports from the Paris–Taiwan and London groups are clearly preliminary, it would seem that the use of bungarotoxin is well grounded on pharmacological evidence. These findings thus offer a great potential for future studies on the molecular mechanisms involved in drug–receptor interaction. Pharmacologists and molecular biologists may be justified in wondering whether this does not constitute at least a partial redemption for the serpent.

Aftermath of the Revolution

THE importance of the article by Baker and Wohlenberg on page 538 of this issue of *Nature* lies as much in the philosophy behind it as in the geological and geophysical knowledge it embodies. For it acknowledges that geology is coming to terms at last with the global model of the Earth which geophysics has imposed on it; and it marks the end of the fear that the vast intellectual edifice constructed by geologists since the ages of Hutton and Lyell must be completely demolished in the light of the new global tectonics. The reality is, of course, far less severe than the fear. For a century or more geologists were much concerned with detailed examination of small regions of the Earth's surface, from which they would attempt to generalize to the larger world. The problem was that, through no fault of their own, they were never able to generalize successfully to the extent of constructing a valid world model. That geophysicists have in less than ten years been able to do just that proves not so much that the geologists were wrong but only that the tools at their disposal were not up to the task.

The way ahead is thus not to destroy the old geology but to reinterpret its legacy in terms of the new global tectonics. And to their credit, Baker and Wohlenberg have recognized this. The purpose of their article is, they say, "to summarize modern geological knowledge of the Kenya rift and to reconcile this with crustal models and kinematic concepts derived primarily from geophysical data". They are surely right in seeing this as the logical procedure to follow in the wake of what J. Tuzo Wilson has so aptly termed the revolution in the Earth sciences.

The scientific point to emerge from the reconciliation is not perhaps the surprise it would have been a few years ago. Baker and Wohlenberg conclude that although the East African rift is linked to, and at first sight seems to be a continuation of, the world oceanic ridge system, it is neither typical of that system nor probably an example of the first stage of continental breakup. In rejecting the idea that rift valleys are the simple land based equivalents of the median valleys of oceanic ridges, and in attributing the former instead to "long-continued interaction between crust and thermally activated mantle", Baker and Wohlenberg have thus followed a different route to arrive at a conclusion similar to Murray's (*Earth Planet. Sci. Lett.*, **9**, 34; 1970), which was based on geochemical evidence. At the same time they confirm the suspicions generated by the discovery that the heat flow over the East African rift is, if anything, lower than the world average and not abnormally high as over oceanic ridges.

There is, of course, some irony in that although Baker and Wohlenberg have enthusiastically embraced the new global tectonics, they have been instrumental in destroying one of its most cherished myths. But there is no harm in that. If geophysicists have a fault it is that they have sometimes tended to exaggerate the extent to which the simple tenets of global tectonics apply to the real world. So there is nothing to be lost by a few counterbalancing jolts from time to time. It is a pity, though, that when Baker and Wohlenberg wrote their article they did not have at their disposal the seismic refraction and gravity data from the Gregory rift described a few weeks ago by Griffiths *et al.* and Khan and Mansfield in *Nature Physical Science* (**229**, 69 and 72; 1971). The crustal model proposed by Khan and Mansfield, in particular, is somewhat different from those proposed earlier; and to this extent Baker and Wohlenberg may have wished to revise some of their details in the light of the new evidence.

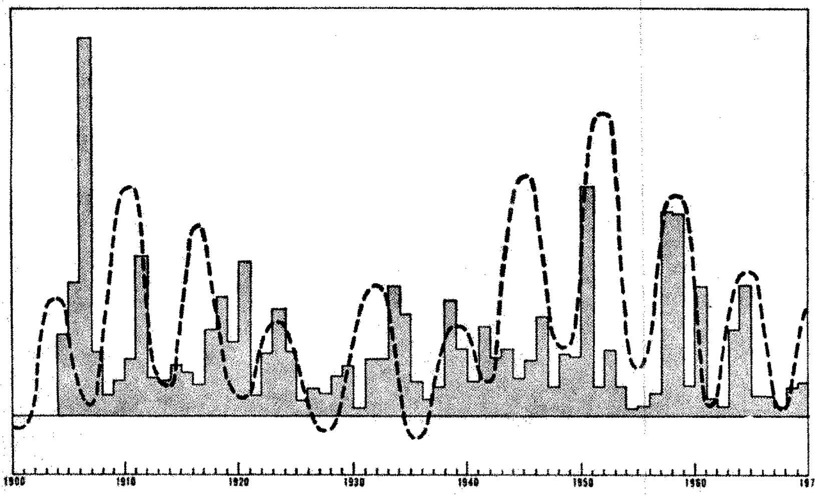
Surprisingly, perhaps, the seismic refraction study of the Gregory rift carried out recently by Griffiths *et al.* was the first attempt to determine the detailed crustal structure in this region. In spite of the widespread interest in the East African rift, first as an extension of the worldwide system and now because it is thought to be in some respects different from the rest of the system, the amount of work done there is remarkably small. Which is a pity. For one reason or another the large American geophysical community has never taken much interest in this important region; and what studies there are have been carried out chiefly by British and Kenyan scientists working either separately or in collaboration.

In view of the importance of finding out just what are the differences and similarities between the East African rift and the oceanic ridges, the time has surely come to mount a geophysical and geological attack on this region.

EARTHQUAKES

More Correlations

from our Geomagnetism Correspondent



The correlation of mean daily polar shift (dotted line) with annual energy released by earthquakes (hatched area).

Correlations between very large earthquakes and sudden changes in the centre of Chandler wobble by Mansinha and Smylie (*J. Geophys. Res.*, **72**, 4731; 1967) certainly seem to have generated a renewed interest in what, superficially, may seem a dull and not very important problem. As a result of their discovery Mansinha and Smylie suggested that the Chandler wobble may, in fact, be maintained by earthquake energy, though Ben-Menahem and Israel (*Geophys. J.*, **19**, 367; 1970) soon showed that this could not be so. Then Myerson entered the field (*J. Geophys. Res.*, **75**, 6612; 1970) with correlations between the yearly count of earthquakes with magnitudes greater than 7.0 and the rate of change in the Chandler amplitude squared; and concluded from this that although the Chandler wobble may not be a direct result of earthquakes, both phenomena could well be consequences of a third.

This upsurge of interest in an old problem now seems to have affected Whitten (*Earthquake Research in ESSA 1969–70*, p. 7, US Government Printing Office, 1970). Just how Whitten acquired his enthusiasm for this topic is in itself an interesting phenomenon and throws a fascinating light on how scientists come to the problems they try to solve. In 1969, it seems, Whitten attended a conference at which Mansinha and Smylie's work took pride of place and was moved to study the problem himself—with some interesting consequences. The Chandler wobble has a period of about 14 months; but there is also an annual wobble term which has a different origin. Whitten noticed that in order to get at the Chandler wobble proper Mansinha and Smylie had subtracted out the annual term. There is, of course, nothing wrong with that. Mansinha and Smylie were only interested in the cause of the Chandler wobble and thus tried to eliminate the non-Chandler contribution to the polar shift. As Whitten points out, however, the Chandler and annual wobbles cannot be separated all that neatly; and so he decided, instead, to compare the energy released by earthquakes with the total daily polar shift.

When the 12-month and 14-month wobbles are out of phase with each other the daily polar shift is very small because the amplitudes of the two wobbles are similar. But when the two wobbles are in phase the daily motion can be as high as 15 cm. The combination of the Chandler and annual wobbles thus causes a variation of daily polar shift with a periodicity of about 7 years. What Whitten has discovered is that there seem to be more large earthquakes when polar motion is at a maximum (see diagram). To be sure, the correlation is not perfect—particular anomalies are the San Francisco earthquake of 1906 and the Chile earthquake of 1960.

What this says about the cause of Chandler wobble or of earthquakes is not clear. Whitten is inclined to believe that the daily angular shift of the axis of rotation could create additional strains in seismic regions and thus acts as a triggering mechanism. Be that as it may, the consequences of Whitten's correlation in terms of earthquake prediction are even more significant, for we are now at about maximum polar shift. With three large quakes within the past month, Whitten's diagram becomes very interesting indeed.

Free-Radical Substitution at Metal Atoms

Bimolecular homolytic substitution reactions of the type $A\cdot + B{-}C \rightarrow A{-}B + C\cdot$ are common in organic chemistry. A, B and C represent atoms or groups. B (the group transferred) is usually hydrogen or a halogen atom; it can (less commonly) be an oxygen or sulphur group. Direct substitutions at saturated carbon rarely occur.

In next Monday's *Nature Physical Science*, Davies and Roberts of University College, London, argue that S_H2 reactions of this type are very common at metal centres in organometallic compounds, and that most involve the displacement of an alkyl radical $R\cdot$ from a non-transition metal compound MR_n by a radical $X\cdot$.

$$X\cdot + MR_n \rightarrow XMR_{n-1} + R\cdot \qquad (1)$$

Examples of radicals which can effect S_H2 reactions include alkylperoxy, alkoxy, sulphur, dialkylamino, succinimido, and alkyl radicals, as well as halogen atoms. A wide range of organometallic metal atoms can be attacked and boron and tin compounds feature prominently. Direct evidence for reactions such as (1) is provided by ESR studies; for example t-butoxy radicals will displace alkyl radicals from boron trialkyls. The alkyl radicals can be detected by ESR, and this seems to be a useful method for production of specific organic radicals.

There is a great deal of evidence that autoxidation of boron trialkyls and other organometallics occurs by a radical chain reaction (reactions 2 and 3), in which reaction 2 is an S_H2 reaction on the metal atom.

$$R'{-}OO\cdot + BR_3 \rightarrow R'OOBR_2 + R\cdot \qquad (2)$$

$$R\cdot + O_2 \rightarrow ROO\cdot \qquad (3)$$

Autoxidation of hexa-ethylditin is thought to proceed analogously; an $Et_3SnOO\cdot$ radical is assumed to displace an $SnEt_3\cdot$ radical from $Et_3Sn{-}SnEt_3$.

The reaction of N-halo-succinimides with tetra-alkyltins is interesting. A chain mechanism is postulated (Suc· is the succinimide radical).

$$Suc\cdot + R_4Sn \rightarrow Suc{-}SnR_3 + R\cdot \qquad (4)$$

$$R\cdot + Suc{-}Hal \rightarrow R{-}Hal + Suc\cdot \qquad (5)$$

A number of reactions of halogen atoms are interpreted in terms of S_H2 attack at metal centres, for example the reactions with organomercurials; heterolytic mechanisms often compete in these reactions. Alkyl radicals seem to attack metal centres by S_H2 reactions (for example, boron, silicon, tin and mercury).

Davies and Roberts conclude that recognition of S_H2 mechanisms frequently offers the key to understanding familiar organometallic reactions and to the prediction of new ones. Physico-chemical studies are needed to discover the way in which electronic and steric effects control the rates of these reactions.

ARCTIC GEOLOGY

Basin Drift

from our Structural Geology Correspondent

THE declared theme of the symposium on Arctic geology, organized by the American Association of Petroleum Geologists and held in San Francisco during February 1–4, was the regional geology of the Arctic. This subject was convincingly and comprehensively covered by some thirty contributors, but most interest was perhaps aroused by the discussions of petroleum exploration and the evolution of the Arctic Ocean Basin.

At the time of the 1960 symposium ideas of seafloor spreading and the associated concept of plate tectonics were in their infancy. Consequently many of the earlier hypotheses for the evolution of the Arctic Ocean Basin have had to be substantially modified. As pointed out by Dr N. A. Ostenso (Office of Naval Research, Arlington), the unique situation of the Arctic Ocean, bordered by both the New and Old Worlds and linking the Atlantic Ocean with the Pacific Ocean, presents a key to understanding not only the present spreading movements but possibly also the older plate arrangements.

The Arctic Ocean consists of two distinct oceanic basins—the Eurasia Basin and the Canada Basin, separated by a strip of continental crust, the Lomonosov Ridge. The Eurasia Basin was shown by means of symmetrical magnetic anomaly striping to have opened during the past 30 million years; its central spreading ridge was connected by means of the De Geer transform fault to the mid-Atlantic spreading ridge. The Lomonosov Ridge would thus represent a piece of the Barents Shelf carried westwards by spreading. The Canada Basin seems to be an older oceanic basin with no pronounced magnetic striping. Views concerning its origin were varied, but most speakers, including Dr I. L. Tailleur (US Geological Survey), favoured its opening during Late Mesozoic by means of a pivotal action about the Alaskan Orocline which would have involved the rotation of Alaska away from the Arctic Canadian Islands, a situation well substantiated by surface geology.

Baffin Bay and its connexion by way of the Davis Straits to the Labrador Sea and the Atlantic was shown (J. W. Kerr (Geological Survey of Canada), and others) to have opened by the drift of Greenland away from Baffin Island pivoted on Ellesmere Island in the Canadian Arctic. Thus the present Arctic Basin seems to have developed during the most recent stages of seafloor spreading, in contrast with the Pacific which it would seem presents a constant physiogeographic feature at least since the beginning of Phanerozoic time.

Measuring the Invisible

FIFTY years ago a distinguished Rolls-Royce engineer, A. A. Griffith, postulated an explanation for the fact that the tensile fracture strength of brittle solids such as glass is surprisingly low and moreover statistically very variable. He proposed that the surface is pitted by many submicroscopic cracks which can locally amplify an applied stress.

Circumstantial evidence has long since established Griffith's hypothesis beyond all cavil. Practical improvements in the strength of glass and other brittle materials have been based on Griffith's recognition that the surface determines strength; strength can be increased by either removing the cracks through etching or otherwise, and at once protecting the surface by means of a hard coating, or by prestressing a thin surface layer in compression.

Throughout all such technological developments, Griffith's microcracks have remained shadowy entities, apprehended but not seen. A number of methods have been tried to make them visible: plenty of cracks were revealed, but there are reasons for believing that the treatment may create more new cracks than it enlarges old ones.

Next Monday's issue of *Nature Physical Science* includes an article by J. D. Poloniecki and T. R. Wilshaw which establishes a new way of tackling the problem. The technique is the Hertzian fracture test. A hard sphere (here a tungsten carbide ball 0.77 mm in diameter) is pressed into the glass surface under continuous observation until a ring crack suddenly spreads and grows concentrically with the indentation. The radius of this crack, r_c, and the load P at which it forms are recorded, and the test is repeated many times. The ring radius and critical load are related to the surface density of microcracks of various depths, and therefore in principle it is possible, from distributions of r_c and P, to deduce histograms of surface densities of cracks as a function of crack-depth. This has been recognized for some years, but the problem has been to find an acceptable way of analysing the data statistically. Most previous investigators have been content to postulate a particular form for the histogram (a "Weibull distribution"), which prejudges the central issue. Moreover, nobody has proposed simultaneous analysis of the distributions of both r_c and P.

Poloniecki and Wilshaw's investigation is the outcome of a collaboration between a fracture mechanics expert and a statistician, and it now seems that the analytical problem has been solved. The critical step is to assess the surface area "at risk" in each individual test, and to sum these for all the tests: this total area at risk is different according to the particular range of crack depth under assessment, and has to be separately estimated for each bar of the histogram. The technique has been applied to mechanically polished silica glass and a log/log histogram produced, complete with 90 per cent confidence limits.

Source Counts and Astronomical Evolution

THE game of counting astronomical sources as a function of brightness to test whether they are distributed uniformly throughout space seems to have been invented by Newton.

In the 1960s, the radio astronomers, after a false start based on the ill-starred second (2C) Cambridge catalogue, agreed that they had shot down the steady state theory with radio source counts. The 4C and 5C surveys showed, however, that the unexpectedly steep increase in the number of sources with decreasing brightness did not continue indefinitely, and in fact were at first interpreted as implying that we had seen right back to the epoch at which the galaxies giving rise to the radio emission were formed. This would have been a spectacular result, but unfortunately turned out not to be the only possible interpretation of the source counts.

When the results of the deep Cambridge surveys were confirmed by counts performed by the radio astronomy group at Bologna, it looked as if the observational situation, at least, was sewn up. A cloud appeared on the horizon recently in the form of counts of 8,100 sources surveyed by the group at Ohio State University (Harris, Beverly and Kraus, *Nature*, **227**, 785; 1970). The OHS surveys were done at a slightly different frequency to those at Cambridge and Bologna (1,415 MHz instead of 408), but on conversion they gave significantly fewer faint sources than the latter, though agreeing in the number of bright sources.

In next Monday's *Nature Physical Science* Jauncey and Neill of Cornell University describe some observations which seem to clear up the discordance. Using the NRAO 300 foot dish, which at 1,400 MHz has considerably better resolution and sensitivity than the OHS instrument, they have checked the OHS flux density scale. They found that the random errors are greater than those quoted (which would tend to increase the number of faint sources found) and, more importantly, that the flux densities of the weaker sources are systematically underestimated. This latter bias was confirmed by comparing the OHS catalogue with others done at the same frequency at Cal Tec and at Parkes. Correcting for the bias brought the source counts into agreement with the Cambridge and Bologna counts.

PULSAR MODELS

Agreement at RAS

by our Cosmology Correspondent

In only three years pulsars have been reduced from the centre of attention among astronomers to the mundane level of routine work. This rapid decline was clearly evident at the specialist meeting on pulsars held by the Royal Astronomical Society on February 12, which contrasted sharply with the first RAS meeting after the announcement of the discovery of these unusual radio sources, or, more recently, with the similar specialist meeting on X-ray astronomy held in November last year (see *Nature*, **228**, 715; 1970). At these earlier meetings, there was a great deal of variety in the ideas and observations presented, with many questions and other contributions from the floor. But at the more recent gathering, only different versions of the same basic model were presented, and very few new observations. The magic word "pulsar" still had sufficient charisma to attract a large audience, but this remained on the whole passive, so that the individual speakers and the whole meeting ran almost exactly to the planned schedule—a very unusual occurrence, and one which is not necessarily a good sign.

Before discussion of the theory of pulsar mechanisms, Professor F. Graham Smith (Jodrell Bank) presented the by now familiar data obtained from the addition of many successive pulses from a pulsar, which seem to show a variation of pulse arrival time over a "window" which remains constant and very well defined. Together with the polarization evidence, this suggests strongly that the regions producing pulsar radiation are confined to a local area (covering some 10° in longitude) on the underlying neutron star; the size of this allowed area defines the observed window, and the small degree of variation in longitude within this region can explain the secular variation frequently observed over several successive pulses. Presumably, this variation is related to the degree of flexibility in the magnetic field which is now almost universally accepted as the beaming mechanism.

The first person to present the pulsar model was Professor L. Mestel (University of Manchester), who made the most of his opportunity to address a still receptive audience, outlining the oblique rotator model which stands unchallenged because of its ready explanation of the timing mechanism of pulsars. This model is based on the natural assumption that a rotating neutron star may have an associated magnetic field, and that the magnetic polar axis is unlikely to be the same as the star's spin axis. It is equally implausible that the magnetic axis would be at right angles to the spin axis, but consideration of these two extreme cases shows how the more probable intermediate cases may produce interactions leading to beamed radiation.

Streaming of charged particles outwards along the magnetic lines of force in this kind of model naturally leads to a situation where they are moving in a circle close to the speed of light, because although the magnetic field may lag behind the solid rotation of the underlying neutron star it must rotate almost as a solid body. Rotation at constant angular velocity then implies that sufficiently far from the star the field is rotating at the speed of light. The silent majority seemed happy to accept this idea as a now well established fact, especially when it was presented three times in rapid succession, with only relatively minor problems remaining to be solved. In one interpretation, the outward flow of plasma only reaches relativistic velocities (and produces beamed synchrotron radiation) where the magnetic field is travelling at twice the speed of light, and there was some discussion of the detail of the kind of magnetosphere which would agree with the observed radiation. To an outside observer the fire and excitement has definitely gone out of the pulsar hunt. Indeed, the experts are so blasé that they accepted the news that the Crab pulsar's so-called precursor pulse is completely absent at a frequency of 606 MHz (see *Nature Physical Science*, **229**, 192; 1971) without comment, even though this pulse is the strongest of the three seen in NP 0532 at half this frequency.

Identification of *X* and *Y*-bearing Human Sperm

It has been shown recently that some fluorescent dyes such as quinacrine mustard stain certain chromosome regions in a specific fashion. Of particular interest is the discovery that the distal end of the long arm of the human *Y* chromosome has a very characteristic fluorescent band (L. Zech, *Exp. Cell. Res.*, **58**, 141; 1969) enabling its detection in mitotic and meiotic cells as well as in interphase nuclei. Last year, two groups of workers (P. L. Pearson and M. Bobrow, *J. Reprod. Fert.*, **22**, 177; 1970; and P. Barlow and C. G. Vosa, *Nature*, **226**, 961; 1970) reported that slightly less than 50 per cent of mature human sperm stained with quinacrine contain a fluorescent spot and these were tentatively identified as *Y*-bearing sperm.

In next Wednesday's *Nature New Biology*, Sumner, Robinson and Evans report their findings from a study of sperm from nine chromosomally normal individuals. Their results confirm that just under 50 per cent of mature sperm contain a fluorescent spot. In view of the fact that the human *X* chromosome is much larger than the *Y*, they point out that *Y*-bearing sperm should contain significantly less DNA than *X*-bearing ones. Using fluorescent staining followed by optical density DNA measurements, they show that the sperm with the fluorescent spot do indeed contain significantly less DNA than those without fluorescence. This optical density difference is of the order of just below 3 per cent and fits in well with the estimates of approximately 4 per cent from published linear measurement of metaphase chromosomes as the difference in length and thus presumably in DNA content between the *X* and the *Y* chromosomes. The present DNA measurements thus confirm the value of the fluorescent technique in distinguishing *X* and *Y*-bearing sperm.

In addition to the two major classes of sperm Sumner and his colleagues note that a small proportion (1.26 per cent) have two fluorescent spots and a DNA value intermediate between the *X* and *Y*-bearing classes and conclude that these are 24,*YY* sperm which have arisen from *Y* chromosome nondisjunction at the second division of meiosis. The complementary product of such a nondisjunction would be a sperm with a haploid autosome set and no sex chromosome. These two types of abnormal gamete would, if successful in fertilization, give rise to 47,*XYY* and 45,*X* zygotes. If all the 1 per cent or so of 24,*YY* and a similar number of sex chromosome deficient sperm were as successful at fertilization as normal sperm, a similar proportion of both 47,*XYY* and 45,*X* zygotes might be expected. Studies of live newborn populations indicate an incidence of 0.8 per thousand live births for 47,*XYY* and 0.2 per thousand live births for 45,*X* individuals.

The *XO* sex chromosome complement is a very notable contribution to foetal loss (approximately 7 per cent of all spontaneous abortions), but a 47,*XYY* complement has not been described in an abortus. Because of the discrepancy between the proportions of presumptive 24,*YY* sperm and 47,*XYY* live births, and taking into account that there is no evidence of 47,*XYY* foetal loss, the authors conclude that 24,*YY* sperm have a reduced capacity for fertilization compared with normal sperm. This is of interest, as is the fact that there is a great excess of female 18-trisomic (47,*XX*,18+) newborns and also a small excess of female abortuses with this trisomy suggesting that disomic-18 *Y*-bearing (24,*Y*,18+) sperm may be at a similar disadvantage.

The authors have also studied sperm from bull, rabbit and mouse and meiotic and mitotic cells from rabbit and mouse and found no strongly fluorescing chromosome in these species.

BACTERIOPHAGES

Peaceful Coexistence

from our Cell Biology Correspondent

Coliphages which peacefully coexist with, rather than kill, *Escherichia coli* cells seem to be comparatively rare—although, of course, this may well reflect nothing more significant than the selective sampling of molecular biologists—and they are comparatively poorly understood. Such phages, and fd is the most familiar, are, however, attracting increasing attention. For just as the lytic phages have proved to be ideal tools for probing many of the basic processes of gene expression—the discovery of messenger RNA and much that has followed depended on their availability—so such coexisting phages as fd may prove equally useful for probing second order biological processes. Particles of fd, for example, are apparently assembled as they pass across the bacterial cell envelope rather than in the infected cell's cytoplasm; the secretion of fd particles may well therefore be a useful model system for studying the movement of large molecules across membranes. Cells infected with fd also provide a system for investigating the continued replication of two replicons, the bacterial and viral chromosomes, in one cell.

Marvin and his colleagues (Hohn, Lechner and Marvin, *J. Mol. Biol.*, **56**, 143; 1971) have been looking at the latter problem and have come up with a model for the replication of fd, which, although similar to that proposed by Sinsheimer to account for the replication of φX 174, has some unique features. The pattern of incorporation of 1 minute pulses of thymidine into fd and bacterial DNA during the first hour after infection is consistent with the model of the replication of φX 174 DNA which fd DNA closely resembles. The single stranded and circular fd DNA is first converted to a closed, circular and double stranded replicative form (RF1). This, attached to some membrane site, replicates to produce progeny RF1 molecules. The model for φX 174 replication envisaged that only the RF1 molecules, retaining a parental strand of DNA from the infecting particle, remain attached to membrane and able to replicate. Hohn *et al.* suggest, however, that in the case of fd replication all the RF1 molecules are able to replicate semiconservatively because they observe an exponential increase in the rate of DNA synthesis at this stage in the replication cycle. Eventually the RF1 molecules, instead of replicating semiconservatively, begin to act as templates for the asymmetric synthesis of single strands of progeny viral DNA which can be incorporated into progeny virus. Hohn *et al.* propose that this switch from double to single stranded DNA synthesis is brought about by the product of fd gene 5, which is known to be essential for the synthesis of progeny single strands but not RF1 molecules. They suggest that this gene product somehow specifically inhibits the replication of one of the two strands of fd DNA, thereby generating single stranded molecules and preventing these from being converted into double stranded RF1 molecules.

Hohn, von Schutz and Marvin (*ibid.*, 155) have also examined what happens in cells infected and killed by fd because the secretion of progeny particles is inhibited. In such a situation, which they call abortive infection, the input fd genomes are converted to RF1 molecules but by the end of this latent period bacterial DNA synthesis, RNA synthesis, protein synthesis and ATP generation are inhibited although the synthesis of bacterial membrane seems to continue. The product of the fd gene 2 plays a part in this killing because fd mutants with an amber mutation in this gene do not kill *E. coli* which are prevented by one means or another from secreting progeny phage. The gene 2 product is also required for the replication of double stranded viral DNA and it is probably bound to the bacterial membrane. Hohn *et al.* suggest from all this that in abortive infection the gene 2 product interacts with the bacterial membrane in such a way as to shut off respiration, believed to be a membrane associated function, and kill the cell. Killing by fd, as well as the secretion of fd in normal infections, may therefore provide new experimental approaches to the structure and function of the bacterial envelope.

Methionine initiates Adenovirus Proteins

This time last year few biochemists would have readily agreed that methionine is the first amino-acid laid down at the start of synthesis of proteins in the cells of higher organisms as well as in bacteria. But in the past year it has been conclusively shown that haemoglobin, protamines in the cells of trout testis and polypeptides synthesized in an ascites cell-free system programmed with EMC virus or synthetic messenger RNAs are all initiated with a methionine residue. Methionine seems indeed to be the universal initiating amino-acid and the report by Caffier, Raskas, Parsons and Green, in next Wednesday's *Nature New Biology*, that eight or nine adenovirus proteins are initiated with this amino-acid should prove that this generalization is not over-optimistic.

Caffier *et al.* prepared cytoplasmic extracts of KB cells (a line of human carcinoma cells) infected with adenovirus type 2. These extracts support the synthesis of eight structural proteins of adenovirus particles and possibly a ninth adenovirus protein which is not part of the virion. The first amino-acid of the eight species of structural proteins, as isolated from virus particles, is either alanine or glycine but in no case is the first, N-terminal, amino-acid methionine. To test whether alanine or glycine rather than methionine are the amino-acids which actually initiate the synthesis of these proteins in their cell free system, Caffier *et al.* assayed the incorporation of methionine donated by an initiating methionine transfer RNA isolated from yeast and added to the cell free system. At least 60 per cent of the methionine incorporated into nascent adenovirus proteins, and 35 per cent of the methionine found in completed and released proteins was at the N-terminal position. Clearly in this artificial situation methionine initiator transfer RNA from yeast can initiate the synthesis of adenovirus proteins. But is methionine the initiator in intact KB cells not supplemented with yeast transfer RNA?

To answer that question Caffier and his colleagues compared the uptake of methionine by adenovirus 2-infected KB cells exposed to a 5 minute pulse of H3 methionine and by their cell free system exposed to a 20 minute pulse of H3 methionine. In both cases, 25 per cent of all the methionine found in nascent adenovirus proteins was at the N-terminal initiating position whereas in completed and released proteins 5 per cent of the methionine was found to be N-terminal. These results strongly suggest that in KB cells adenovirus proteins are initiated with methionine. On average there are fourteen methionine residues in these eight adenovirus proteins. If the synthesis of each began with methionine and if the methionine was not cleaved from the chain until after it was completed and released, about 7 per cent of all incorporated methionine residues would be N-terminal. This is close to the observed 5 per cent, which suggests not only that all these adenovirus proteins are probably initiated with methionine but also that many of the initiating methionine residues are not cleaved until after the protein has been completely synthesized.

One other interesting detail emerges from this work; yeast initiator transfer RNA carrying a methionine residue which is formylated (with a formyl group on the amino-group of methionine) does not initiate adenovirus proteins. This result, in keeping with those of Smith and Marcker and others, indicates that it is a methionine residue, rather than an amino-acid with a blocked amino-group, which is universal to chain initiation.

GLYCOGEN BREAKDOWN

Enzyme Ensemble

from our Molecular Biology Correspondent

CHARGAFF'S deathless adage that molecular biology is merely biochemistry practised without a licence may seem to find support in comparisons with work such as that of Fischer, Krebs and others on the system of enzymes responsible for the breakdown of glycogen. What at best characterizes the thinking of the fully licensed practitioner, and is so striking a feature of this work, is the manner in which the objectives and results are related to the broad biological design, and are brought ever closer to the situation in the cell. The latest successes in this direction are described in three massive articles from Fischer's laboratory on the interrelation between the enzymes of glycogen breakdown in newly discovered subcellular particles prepared from muscle.

The breakdown of glycogen, in accordance with instantaneous energy requirements, is controlled by the activity of glycogen phosphorylase. This enzyme exists in two states: phosphorylase *b*, at least *in vivo* at high concentration, is a form of low activity, which is activated to a modest degree by AMP. Under the action of phosphorylase kinase it is phosphorylated at one serine residue in each of the four subunits, to give the highly active phosphorylase *a*. The kinase is itself activated by calcium ions, with the additional complication that a calcium-dependent protease, present in the tissue, also causes activation, perhaps adventitious, of the kinase by limited proteolysis. To complete the cycle, the *b* form is regenerated from the *a* by the action of a phosphatase, which is liable to inhibition by nucleotides.

Meyer *et al.* (*J. Biol. Chem.*, **245**, 6642; 1970) now show that all these enzymes coexist in glycogen particles, 200–300 Å in diameter, which can be prepared in several ways from muscle. The preparations also contain much larger vesicles, apparently derived from the sarcoplasmic reticulum. These can be separated from each other by sedimentation or gel filtration, and the phosphorylase and its satellite enzymes appear in the smaller glycogen particles, whereas the vesicle fraction contains highly active calcium pump ATPase.

In the second article (Heilmeyer *et al.*, *ibid.*, 6649) the mechanism of control of phosphorylase activity in these particles is examined. The phosphorylase *in situ* is entirely in the *b* form, and thus essentially inactive. The phosphorylase kinase is also dormant, but the phosphatase is active, so that no conversion to phosphorylase *a* is possible. When now magnesium ATP and calcium are added, there is a rapid and spectacular eruption of phosphorylase activity, far too large to be put down to nucleotide activation and, as the absolute requirement for calcium ions shows, caused by the revival of the phosphorylase kinase. After an interval, depending on the ATP concentration—for this is quickly depleted by contaminating ATPase—the phosphatase regains the upper hand, and the phosphorylase activity vanishes.

In the third paper, Haschke *et al.* (*ibid.*, 6657) consider the rôle of phosphorylase phosphatase. They find that magnesium ATP and calcium, the very agencies responsible for unleashing the kinase, also inhibit the phosphatase. The build-up of AMP and the deamination product, IMP, which are both inhibitors of the enzyme, is altogether insufficient to account for the effect. In the absence of evidence to suggest chemical modification it seems likely that there is another inhibiting component in the glycogen particle that regulates it.

BACTERIOP

Another E

by our Molecular Ge

DEFINING completely t chromosome of a livin comparatively so simple as is obviously going to take time indeed. But accounting function coded by a viral gen be a more practical proposition. come in many sizes and shapes, of course, and the trick of success may perhaps be to pick one with the right order of complexity. As lambdologists will ruefully vouch, even a comparatively small virus such as lambda, which has about fifty genes, has a bewildering number of control systems which are proving all too difficult to disentangle.

The very small phages have genomes which are RNA or single stranded DNA;

Evolving Histones?

IN the past few years histone chemistry has rapidly emerged from the dark ages of not so long ago when histone chemists spent their lives arguing about each others' artefacts. It is true that the function of histones is almost as obscure as ever, but today such is the sophistication of protein chemistry that arguments now centre on the possible evolutionary relationships between histones of known amino-acid sequence rather than on how to fractionate reproducibly various types of histones. Indeed, one type of histone, fraction IV, provides the outstanding example of the evolutionary stability of a protein. Fraction IV histones of pea cell nuclei and calf thymus cell nuclei differ in sequence by only two amino-acids. How long is it since cows and peas diverged from a common ancestor? Such striking evolutionary stability is a characteristic of several types of histone from diverse sources; on the other hand there is evidence that certain histones are species and even tissue specific. Fraction V histones are the best example; these are uniquely restricted to red blood cells, but as Greenaway and Murray speculate in next Wednesday's *Nature New Biology*, fraction V histones may be ancestral to the fraction I histones of other cell types.

Greenaway and Murray noticed that the fraction V histone of chick erythrocytes can be resolved into two fractions, Va and Vb, by chromatography on 'Amberlite' columns. The two fractions, obtained reproducibly, proved to have the same N-terminal amino-acid, the same electrophoretic mobility and they do not differ in the extent to which they are acetylated, methylated or phosphorylated. In fact, after extensive tests the only difference Greenaway and Murray found between the two proteins was at the position of the fifteenth amino-acid residue in their sequences. Histone Va has a glutamine residue at this position whereas histone Vb has an arginine residue.

These initial experiments were done with histones extracted from the pooled blood from about 1,000 chickens and the obvious question arose as to whether any one bird has both histone Va and Vb. Experiments with the histones from the blood of individual birds showed that they either had histone Vb or both Va and Vb. Furthermore, preliminary analyses of the inheritance of these patterns indicate that in fowl there are probably allelic genes for the two proteins. The existence of chickens homozygous for fraction Vb, however, proves that both alleles are not essential for survival.

The occurrence of such genetic polymorphism among histones increases, of course, the number of distinct histone fractions, but it reduces the complexity of their biological function because such closely related proteins are unlikely to have different functions. Indeed, as Greenaway and Murray suggest, fraction I histones, in cells other than erythrocytes, have so many properties in common with fraction V histones, restricted to red blood cells, that it is quite feasible that fraction I histones have evolved from fraction V histones. If this argument has any truth in it, it follows that fraction I histones have rendered the fraction V histones redundant in all but erythrocytes. The heterogeneity of histone fractions may well belie the range of their functions, which is probably far more restricted than the protein chemist, surveying the numerous fractions from his columns, might be tempted to predict.

or example, ", ph φX 174 or fd NA phages code for nes. These phages must y almost entirely on function their host bacterium. Phage T7, er, which has a duplex DNA ome consisting of nineteen genes, itself codes for several of the activities needed for its infectious cycle, but is not as complex as the larger phages.

This phage has already produced surprises. Gene 1 controls the expression of most of the phage genes; mutants which lack the gene 1 protein product can only make the three earliest T7 proteins. The obvious explanation seemed to be that this gene specifies a phage σ factor (as do comparable genes in the T-even phages) which directs the host cell RNA polymerase to transcribe the late genes of the phage. But T7 differs from the other phages because gene 1 proved to code for a new RNA polymerase, with a specificity for the T7 genes.

Other genes are concerned with specifying the enzymes required to replicate the phage, such as a DNA replicase and a polynucleotide ligase. Genes 3 and 6 are concerned with the degradation of host DNA which provides the nucleotides needed for the synthesis of new phages. The protein specified by gene 3 is an endonuclease which seems to attack both single stranded and double stranded DNA, and Center and Richardson report some of its properties in two articles in the *Journal of Biological Chemistry* (**245**, 6285, 6292; 1971).

The enzyme shows a strong preference for single stranded DNA, which it degrades about 150 times faster than duplex DNA. Its attack on duplex DNA generates single strand breaks, and it is not yet clear just how these are converted into the double strand breaks which are needed to split the DNA. And *in vitro*, at any rate, the enzyme is as active with T7 DNA as template as it is with that from the host *Escherichia coli*. How is the behaviour of the enzyme in degrading only T7 DNA *in vivo* to be reconciled with this apparent lack of discrimination? One possibility is that the product of gene 6, which also seems to be involved in degradation of host DNA, may confer some specificity on the gene 3 endonuclease. Another is that the degradation may take place so soon and so rapidly after the entry of the phage into the bacterium that only host DNA is available for attack at that time; this implies that the endonuclease must be inactivated in some way before replication of T7 DNA generates more substrates for it. At any rate, the gene 3 product has now been unambiguously identified, even if the way it works *in vivo* is not quite clear, and another gene can be ticked off on the list of those whose products are known.

The Helper and the Helped

SORTING out the relationships and interdependence of animal leukaemia and sarcoma viruses is, these days, a chief preoccupation of tumour virologists; for the genome of one RNA cancer virus can be enclosed in the envelope of, and assume, the host range of a second virus. Moreover, many tumour viruses are defective; they have become dependent on the help of a second virus in order to transform and replicate in some hosts. In next Wednesday's *Nature New Biology*, Eckner and Steeves describe just such a situation.

In 1956, Friend isolated from Swiss mice a virus preparation which, when inoculated into mice, either induces an erythroblastic leukaemia, associated with a gross enlargement of the spleen, or a lymphatic leukaemia or lymphoma associated with tumours of the thymus, the outcome of a particular inoculation depending on the strain of mice inoculated. It has since become clear that the Friend isolates contain two viruses, one of which induces lymphomas and the other induces spleen tumours or foci and erythroblastic leukaemia. But what is the relationship between these two viruses; is one a helper for the replication of the other ?

Stocks of the virus which induces spleen foci always contain the virus which induces lymphomas but the converse is not the case. Further, Eckner and Steeves found that the induction of spleen tumours in some strains of mice seems to depend on the multiple infection of the spleen cells by two or more virus particles. These two facts suggest, of course, that the virus which causes spleen foci requires the help of the lymphoma virus, for that would explain both the presence of lymphoma virus in stocks of the spleen focus inducing virus and the observation that the induction of foci depends on multiple infection. But it might be argued that multiple infection somehow impairs the immune system and as a result spleen foci are able to develop. To rule out this possibility, Eckner and Steeves treated mice with cortisol to impair their immune system and found that the induction of foci remained dependent on multiple infection. When, however, stocks of the focus inducing virus were diluted into stocks of the lymphatic leukaemia virus, the induction of foci seemed to be dependent on single infections. In this situation there is clearly a great excess of helper virus; cells are always infected by it so that the induction of foci seems to depend on a single infection by the focus forming particle.

Linkage of Retinal to Opsin

RHODOPSIN, a visual pigment found in vertebrate retinal rods, transduces light into a neural message. It is a chromoprotein and consists of 11-*cis* retinal (retinene aldehyde) and an unspecified protein, called opsin. The two are said to be linked by a Schiff base between phosphatidyl ethanolamine (PE) and retinal, which moves after exposure to light to the ε-amino-group of a lysine residue in the protein. Anderson, Hoffman and Hall question this assumption in next Wednesday's *Nature New Biology*. Is the N-retinylidene-phosphatidyl-ethanolamine (N-RPE) which has been extracted from rod outer segments, and which is dark adapted and then not exposed to light, associated with rhodopsin or not? N-retinyl-phosphatidyl-ethanolamine (N-RH$_2$PE) has also been extracted from rods after acidification of rhodopsin and the sodium borohydrate fixation of retinal to its original site by a secondary linkage. Anderson *et al.* stress that the extracts used contain much phospholipid and retinal not bound to opsin, and they suggest that the isolation of N-RPE may be derived instead from a source other than the retinal–opsin link.

To test if this is so, they measured the turnover of the rhodopsin in the outer segment disks which form part of the rods. They injected frogs with labelled ^{3}H-retinol and then measured the radioactivity three days later from suspensions of their rod outer segments, subdivided into three groups, A, B and C. A was acidified, treated with sodium borohydrate, and was then subdivided into aqueous and lyophilized subgroups. Lipid was extracted from the aqueous subgroup by treatment with a 2 : 1 chloroform–methanol mixture: the separated protein contained 73 per cent of the total radioactivity. The lyophilized subgroup, which had been extracted similarly but without protein partitioning, retained 82 per cent of the activity in the protein. It was found that all the radioactive part which had been removed from the rhodopsin was associated with free retinol, and that no tritium exchange had occurred between it and opsin

Unlike groups A and B, roup C contained rod outer segments originally purified on an 'Agarose olumn. C was subdivided, one half being treated in the same way as A, the other like B; less than 40 per cent of the total radioactivity was associated with the protein and an average of 30 per cent was recovered with N-RH$_2$PE. Anderson *et al.* thus confirm the presence of N-RPE in cetyltrimethylammonium bromide solutions of rod segments, but demonstrate that this lipid forms no part of the rhodopsin chromophore.

Marriage and Fertility in Academic Life

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An analysis of a sample of entries in the 1969 edition of *Who's Who*, suggests that male arts specialists are nearly five times as likely as scientists to remain single.

It has been suggested[1,2] that specialists in the arts and in biological and physical sciences differ not merely intellectually but in personality, and that students perceive these professional groups in the light of simple, highly stereotyped preconceptions[3]. These studies imply that adult specialists in the arts lead relatively uninhibited and unconventional personal lives; that biologists are more conventional, and that physical scientists are more conventional still. The more prosaic and quantifiable aspects of such individuals' personal lives, such as, for example, their patterns of marriage and fertility, have, however, been little studied. Pertinent sources of biographical information[4,5] have also been neglected.

One such source of information is the publication *Who's Who*[6]. This lists, among others, men eminent in British academic life. Fellows of the Royal Society and the British Academy, for example, and professors at Oxford and Cambridge, all receive invitations as a matter of course and few distinguished scholars or scientists are omitted.

Entries in *Who's Who* are completed by the individual concerned, and normally but not invariably include the following information: date of birth, date of marriage(s), number of children and an indication of whether an earlier marriage ended in death or divorce. Details of school and university education, publications, and appointments held are also included. As a biographical source, *Who's Who* is imperfect, but its accuracy bears comparison with responses to interviews or questionnaires, and it offers a rate of response that no other source can rival.

We studied a sample of individuals in *Who's Who* consisting of all those males in the 1969 edition, classified into the following academic groups, who were born between 1900 and 1925, and who had been educated substantially in the United Kingdom. The arts group came from the following fields: philosophy ($n=42$), classics ($n=61$), history ($n=83$) and English literature ($n=30$). The biological science group was drawn from botany ($n=45$), zoology ($n=55$), physiology ($n=20$), genetics ($n=15$), cell and microbiology ($n=12$). The physical scientists came from physics ($n=93$), chemistry ($n=77$), metallurgy ($n=19$), geology and mineralogy ($n=31$) and engineering ($n=109$). The engineers were restricted to those who held senior academic posts, or who were Fellows of the Royal Society. Most of the individuals in each of the three academic groups were professors in British universities and their average age was 57. Ninety-three per cent were married; and of these, 68% had been married for at least 25 years and 94% for at least 15 years.

Table 1 gives the percentages in each of the three academic groups who were single or who had childless marriages. The differences between the three groups are unmistakable. The arts specialists are nearly five times as likely as the scientists to remain single. They are also the most likely to have childless marriages, the tendency, for one reason or the other, to remain childless being particularly marked among classicists (41%). The differences between biological and physical scientists are less marked. Both groups had married in all but a few cases; but the physical scientists are nearly twice as likely as the biologists to have a childless marriage.

These differences in childlessness influence the mean overall fertility rates for the three academic groups: members of the arts group had on average 1.83 children, the biologists 2.50, the physical scientists 2.05. These rates alter relatively little, however, if the groups are restricted to men who have experienced at least 15 years of uninterrupted marriage (2.16, 2.52 and 2.12 respectively).

Table 2 gives the percentages in the arts, biological sciences and physical sciences who married late (age 35 or later) or who have divorced. From these figures, the arts specialists seem to be the group most likely to marry late; half again as likely as the biologists, more than twice as likely as the physical scientists. The pattern for divorce is different. The highest rate was found among the biological scientists: they seem to be three and a half times as likely to divorce as physical scientists, and more than twice as likely as the arts group. In all three groups, divorcees had, on average, more children than others (arts group, 2.70; biologists, 3.05; and physical scientists, 2.45); and in the arts and physical sciences, but not in biology, those married late seemed less fertile (arts group, 1.24; biologists, 2.57; physical scientists, 1.64).

With regard to late marriage and divorce, the arts and biological science groups are each reasonably homogeneous. The physical scientists, on the other hand, contained one obviously discrepant group—the physicists. When compared with chemists, for example, they seem to be six times as likely to divorce. If the physicists are excluded from the sample of physical scientists shown in Table 2, leaving it predominantly a group of chemists and engineers, the physical science divorce rate drops to 1.7%.

It is also interesting that mathematicians ($n=59$, omitted from Tables 1 and 2) differ from all the scientific groups. Their divorce rate seems moderate (3.8%) and their likelihood

Table 1 Proportions of Eminent Men in the Arts, Biological Sciences and Physical Sciences who remain Childless

	Single	Childless marriage	Total
Arts $n=216$	(32) 14.8%	(35) 16.2%	(67) 31.0%
Biological sciences $n=147$	(3) 2.0%	(9) 6.1%	(12) 8.1%
Physical sciences $n=329$	(12) 3.6%	(38) 11.5%	(50) 15.1%

The source of this information ($n=692$) was ref. 6. Frequencies in each of the three columns represent significant deviations from chance: χ^2 test, $P<0.001$, 0.025, 0.001 respectively.

Table 2 Proportions of Eminent Men in the Arts, Biological Sciences and Physical Sciences who Marry Late (35+) and who Divorce

	Marry late	Divorce
Arts $n=216$	(29) 13.4%	(10) 4.6%
Biological sciences $n=147$	(14) 9.5%	(18) 12.2%
Physical sciences $n=329$	(18) 5.5%	(11) 3.3%

The source of this information ($n=692$) was ref. 6. Frequencies in both columns represent significant deviations from chance: χ^2 test, $P<0.01$, 0.001 respectively.

remaining single seems quite high (10.2%) a pattern that identifies them more nearly with the arts group than any other. The social scientists ($n=30$) were another distinctive group omitted from our analysis. A small and by no means homogeneous sample of psychologists ($n=18$), sociologists ($n=5$) and social anthropologists ($n=7$), they are distinguished from other scientists in the study by their high divorce rate (23.3%).

Such evidence, of course, sheds no light on causes; it can as easily be interpreted from biological, psychological, or social points of view. But simple explanations, either in terms of social class or of the biased composition of the *Who's Who* sample, find little support from the data. Although the arts, biological science and physical science groups came in differing proportions from Headmasters' Conference schools (65%, 57% and 37% respectively), and from the Universities of Oxford and Cambridge (74%, 52% and 34%), there seems to be, with one exception, no significant interaction between either factor and the patterns of marriage and fertility within each academic group. The exception lies in divorce among biologists. Those from Headmasters' Conference schools seem more than five times as likely to divorce as their colleagues from grammar schools (19.2% as against 3.6%; χ^2 test, $P<0.025$).

Nor can the results be explained in terms of differences between the academic groups in the number of years they have been married. Although the average ages of the arts, biological science and physical science groups differ slightly (58.1, 59.1 and 56.7 respectively), the length of time since first marriage does not differ significantly between them (χ^2 test, $P>0.1$). Moreover, in science at least, marriage and fertility patterns have no bearing on the level of professional success an individual achieves. If the samples of scientists are restricted to those who are Fellows of the Royal Society, the patterns shown in the bottom two rows of Tables 1 and 2 are not significantly changed. This result supports my earlier findings that the differences between academic fields are easier to predict than success within them[1].

The data summarized here help to substantiate the links between the intellectual realm and those of personality and style of life. Each of the three academic groups seems to have its distinctive pattern. Arts specialists are the most likely to remain single; and if they marry, to do so late and to remain childless. Most scientists seem to marry. Biologists differ from physical scientists in that they are the more likely to marry late, to have large families, and to become divorced.

Broadly, these findings are in keeping with earlier research on the recruitment of scientists, and students' perceptions of them. Not even the discrepant marital patterns of physicists, nor the similarities of mathematicians to the arts specialists are entirely unexpected. Results for the arts specialists conform less well. The high rates for remaining single, for childless marriage and late marriage, and the low rate for divorce are all at variance, superficially at least, both with students' perceptions of the arts and with evidence about the type of student which the arts faculties attract. An interesting complement may be found in the personal lives of novelists, poets and playwrights. The sample of such writers in *Who's Who* is catholic; but a preliminary analysis of the most distinguished suggests a pattern analogous to that of scholars in the arts in all respects but one—divorce. Among creative writers this is very frequent indeed.

Clearly, such results as these cannot form a basis for hasty generalization. The men studied are the eminent few and not necessarily representative of their specialities as a whole—patterns of recruitment, as well as of marriage and fertility, may prove to vary from one country to another, and even from one generation to the next within a given discipline. It is also possible that error has occurred at source, in the shape of omissions from the individual entries in *Who's Who.*

[1] Hudson, L., *Contrary Imaginations* (Methuen, London, 1966).

[2] Hudson, L., *Frames of Mind* (Methuen, London, 1968).

[3] Hudson, L., *Nature*, **213**, 228 (1967).

[4] Galton, F., *Hereditary Genius* (Macmillan, London, 1869).

[5] Webb, J. E., *et al.*, *Unobtrusive Measures: Non-reactive Research in the Social Sciences* (Rand McNally, New York, 1966).

[6] *Who's Who* (Black, London, 1969).

Pozzuoli Event in 1970

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A crustal upheaval near Naples in March 1970 was unusual in not being accompanied by noticeable earthquakes. This could be interpreted in terms of the visco-elasticity of the Earth's crust.

AT Serapeo, on the Bay of Pozzuoli, near Naples, three marble columns, said to be the remains of a Roman temple, provide a record of movements of the Earth's crust since the second century BC. According to Parascandola[1], the floor at Serapeo has subsided by about 11 mm per year (Fig. 1), and been raised several times by calamities. These included the Campanian earthquake in AD 63; the eruption of Vesuvius in AD 79; a mud eruption at Solfatara in 1198; an eruption of Arso on Ischia in 1302; earthquakes felt at Pozzuoli in 1416 and 1488, and in 1536–38, earthquakes followed by the eruption of Monte Nuovo. In Italy crustal movements of this sort have been known as *bradisimi* (slow oscillations) since the nineteenth century. Recently Oliveri and Quagliariello[2] presented a theory of origin of the *bradisismi* at Pozzuoli, interpreting the subsidences as self-loading compactions and the upheavals as variations in the flow of ground water filling porous pyroclastics.

In early 1970, a conspicuous upheaval was noticed at a zone centred on Pozzuoli. At the end of February 1970 some old stone walls at Pozzuoli were cracked by the upheaval and the steaming area of Solfatara increased.

Campi flegrei (fiery fields, Fig. 2) behind Pozzuoli are full of volcanoes, craters, hot springs and steaming fields. The oldest eruption centre which has been dated is Astroni Crater, which erupted about 1500 BC. Next come Fossa Lupara, Concola, Fondo Riccio and Monte Nuovo. In the light of this history of volcanism further eruption might be expected around Pozzuoli.

The most recent event was an anomalous upheaval in March 1970. Changes in height of bench marks around Pozzuoli between 1953 and March 1970 (Fig. 2) show that the maximum upheaval amounted to about 90 cm, assuming that the easternmost point, about 4 km from Pozzuoli, was unchanged. The uplifted zone was circular, centred on Pozzuoli. The upheaval probably began in October 1969.

It is remarkable that no earthquakes were felt at Pozzuoli during the upheaval. Since the end of February 1970 teams from the Institute of Geophysics of the University of Naples and the Vesuvian Observatory have been making seismic measurements in three places at and around Pozzuoli. Usually a few micro-earthquakes of magnitude 0–2 and $S-P$ duration less than 1 s were registered each day. This seems to be remarkably little activity for a time when an anomalous upheaval was in progress, but we have no precise data about normal seismicity there. Earthquake swarms in Japan, however, have been accompanied by crustal movements. The absence of earthquakes in this case could be explained if the upheaval were due to the visco-elastic properties of the Earth's crust. If the upper part of the crust is visco-elastic, one can expect the following two stages: the first when deformation is proportional to the frequency of earthquakes, and the second when there are no earthquakes. The Pozzuoli event may be an example of the latter stage.

The observed upheaval at Pozzuoli can be interpreted by neither of two theoretical curves (Fig. 3) which assume an elastic crust. The curves represent the deformations of a semi-infinite elastic body due to a stress origin buried at a depth of 2 km. Pressure distribution is expressed in spherical harmonics $P_n^m(\cos\theta)$. The observed deformation must be plastic, not elastic.

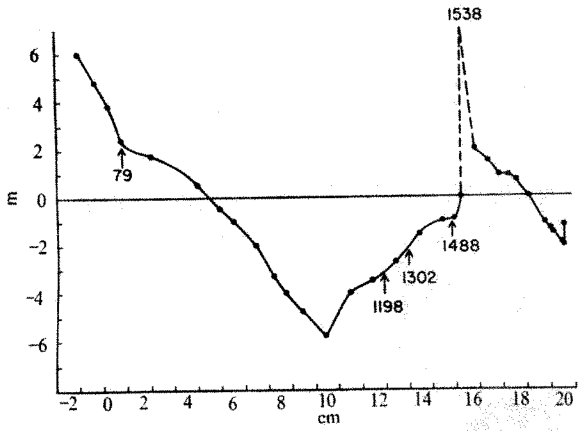

Fig. 1 Changes in height of the floor of Serapeo after A. Parascandola.

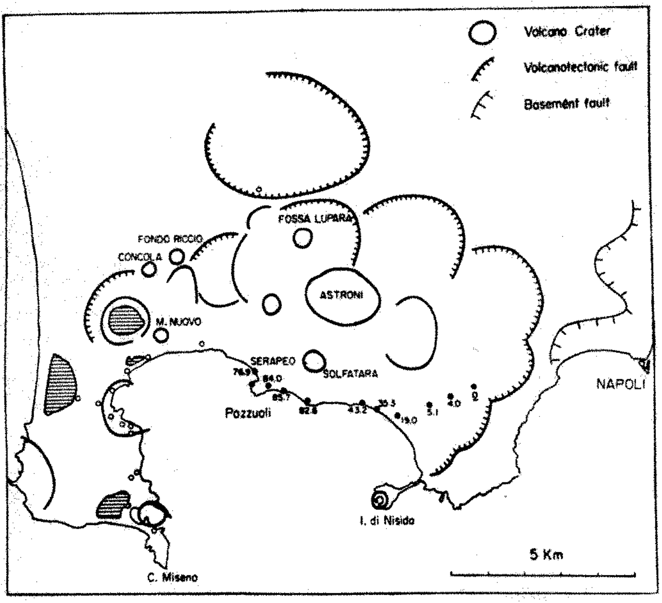

Fig. 2 *Campi flegrei.* Solid and hollow circles denote bench marks for precise levels. Numerals denote the changes in height during the period 1953 to March 1970, after the Provveditorato Opere Pubbliche di Napoli. The unit used is the centimetre.

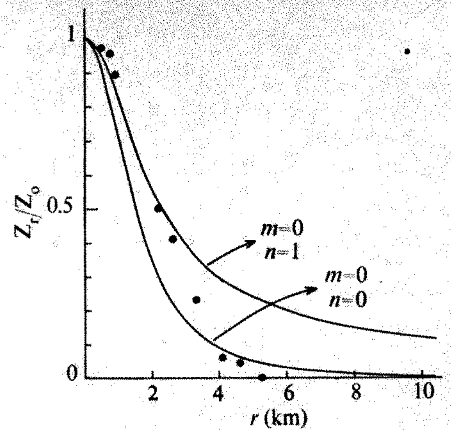

Fig. 3 Relative deformation of surface of elastic body due to a stress origin buried at a depth of 2 km. Solid circles denote the values observed at Pozzuoli ($Z_0=85.7$ cm).

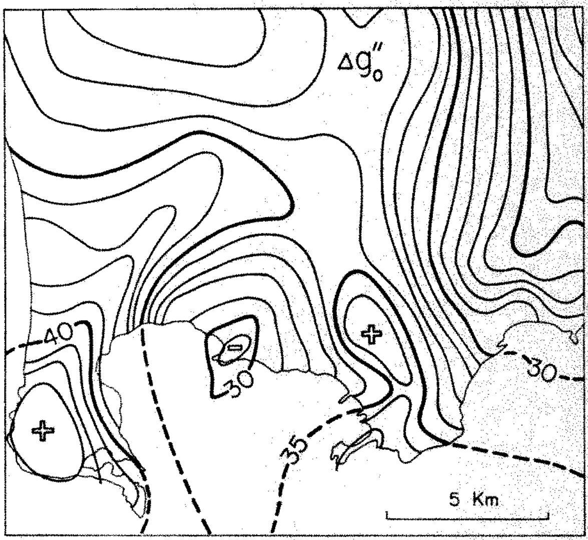

Fig. 4 Distribution of the Bouguer gravity anomalies in mgal., after the Geological Survey of Italy.

The distribution of Bouguer gravity anomalies in this region (Fig. 4) shows that a low anomaly of 7–8 mgal coincides with the centre of the upheaval at Pozzuoli. This may be caused by light deposits (volcanic tuffs) 1–2 km deep at the centre. These deposits would subside continuously as a result of compaction and rise through plasticity, by reacting with hot volcanic material.

According to G. Imbò (personal communication), the phenomena continued slowly after March 1970. The bench mark at the harbour master's office at Pozzuoli rose 14.8 cm between March 1 and June 11, and Nisida Island rose 2.7 cm between March 21 and June 9. This means that a slightly larger area is associated with the *bradisismi* than had been assumed. The seismometers at Pozzuoli registered 256 micro-earthquakes between March 1 and June 10. Almost all were very small, although a few were registered as III or IV on the Mercalli intensity scale.

In conclusion, the rapid upheaval at Pozzuoli, not accompanied by any conspicuous shocks, can be interpreted as a phase of visco-elastic activity in the upper crustal material. Volcanic tuffs would have been affected by some volcanic reactions, such as intrusion of magma or steam. This interpretation does not contrast with the theory of Oliveri and Quagliariello[2].

I thank the Provveditorato Pubbliche in Naples for access to valuable data.

[1] Parascandola, A., *I Fenomeni Bradisismici del Serapeo di Pozzuoli* (Genovese, Naples, 1947).

[2] Oliveri del Castillo, A., and Quagliariello, M. T., *Sulla Genesi del Bradisismo Flegreo* (Atti Ass. Geof. It., XVIII Conv., Naples, 1969).

Uses of Artificial Insemination

by

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Techniques for semen storage and artificial insemination of animals have developed considerably during the past twenty-five years but biological, social and economic factors are still limiting the full development of this technology.

EARLY examples of extra-coital insemination exist in mythology and legend from times when the function of coitus was not understood. For example, Heape[1] referred to a fourteenth century story of an Arab who successfully inseminated his own mare with semen collected from a stallion owned by a neighbouring hostile tribe. But credit for the conclusive successful demonstration of artificial insemination of mammals is due to Spallanzani[2], an Italian priest who worked in the latter part of the eighteenth century. He reported the birth of three puppies after the insemination of a bitch "... artificially in the following manner. A young dog of the same breed furnished (him), by a spontaneous emission, with nineteen grains of seed, which were immediately injected into the matrix, by means of a small syringe introduced into the vagina".

Although Spallanzani's experiments were recognized when he did them, little attempt was made to use the technique until early in the twentieth century when a Russian[3] applied it to mares. After about 1930 it was used with other farm animals and gradually large scale use developed, until the Second World War, after which expansion was rapid. A census during the last decade[4] showed that in one year 59 million cows, 47 million ewes, 1 million sows, 125,000 mares and 56,000 goats were artificially inseminated. Other mammals have been inseminated in fewer numbers (including the domestic dog and cat, water buffalo, alpacas, laboratory rodents, rabbits and so on) and the technique has been applied successfully to birds (for example, 4 million turkey hens inseminated per year)[4], fishes, amphibians and insects. Artificial insemination is used most in the more economically advanced regions and in some countries it is applied to 99 per cent of dairy cows.

The present application of artificial insemination, however, can be misleading, for it has been used for very few of more than 4,000 species of mammals existing and, because successful methods for prolonged storage of semen have only been developed for the rabbit and the domestic cow, it is of limited use for most of those species to which it is currently applied. In this review I shall consider briefly the current methods for artificially inseminating mammals, the problems involved and the future use of the technique. For more detailed descriptions of methods the reader is referred to some[5-8] of the numerous reviews and textbooks available.

So far no harmful effects have been demonstrated, on present or succeeding generations, from the use of preserved semen or artificial insemination. Of course, it must be applied with considerable caution to avoid the development or spread of hereditary faults including sub-fertility. These are some of the advantages of the use of artificial insemination. (1) In the production of livestock it can increase the rate of genetic improvement by expediting progeny testing of males and then increasing the use of superior sires. Its use with dairy cattle in Japan between 1939 and 1962 was associated with an increase in the country's milk production per cow from 2,700 to 4,840 kg[4]. (2) Artificial insemination makes possible better use of crossbreeding livestock. For example, with pigs, it is possible to obtain heterosis to improve grade livestock, to change the form of production—say, from wool to meat producing sheep. With fur producing animals, it is possible to vary coat colour according to fashion and to facilitate the breeding of animals of such different size that natural mating would be difficult, for example the Shire horse and Shetland pony or the great dane and pekinese dogs. (3) Artificial insemination permits hybridization between "species" which would not normally mate or do so only rarely; for example, the fowl and pheasant have been crossed[9]. (4) In veterinary and medical practice artificial insemination facilitates the use of incapacitated or oligospermic males. Banks of deep frozen semen can be used in case of death, and for humans they have been proposed as an assurance against the hazards of war and its consequences, vasectomy and other factors that may affect fertility or the capacity to copulate. (5) Between zoos it would often be preferable, or only possible, to buy semen rather than borrow or buy scarce males and the establishment of semen banks would provide an insurance against the extinction of animal species. (6) The use of artificial insemination is often cheaper and certainly less hazardous than keeping or transporting some large male animals and this is a reason for its rapid acceptance by dairy farmers. (7) Artificial insemination has been used effectively to prevent the transmission of infectious venereal diseases and, for example, was practised in Rumania until 1961 solely to eradicate dourine from the horse[4]. (8) The physiologist finds artificial insemination a valuable tool. It may be used to determine the number of spermatozoa required for fertilization, the correct timing of insemination, comparisons of the fertility of spermatozoa from different males, and many other factors.

Collection of Semen

Semen is usually collected from animals by training the male to serve an artificial vagina[5] or by stimulating ejaculation with an electric current[10]. The success of either method depends on the operator, the preparation of the male and the equipment used. These factors probably account for any differences in the quality of semen collected by either method. Other methods of collection include the injection of drugs[11] to induce ejaculation and masturbation and, if all else is unsatisfactory, the recovery of spermatozoa from the male reproductive tract after slaughter.

The semen of animals[12] consists primarily of spermatozoa and seminal plasma. The numbers of the former and the volume and composition of the latter vary greatly within and between species (Table 1); between individuals of a species they may be affected by such factors as those already stated, frequency of collection and season.

Seminal fluid is a mixture of secretions from the male accessory organs of reproduction (Fig. 1) and differences in volume and composition between species of animals are explained by the possession of varying combinations and sizes of

Table 1 Some Values for the Collection, Storage and Characteristics of Semen

Animal	Quantity per ejaculate Volume (ml.)	No. of sperm $\times 10^{-6}$	No. of inseminations	No. of ejaculates per week	Storage of semen Rate of dilution	Temperature (°C)	Duration
Cattle	4	4,000	400	4	1 : 100	−196	Many years
Rabbit	1	150	20	7	1 : 10	−196	Many years
Man*	3.5	350	2	4	1 : 1	−196	Many years
Goat*	1	3,000	60	14	1 : 4	−196	Many years
Sheep*	1	3,000	60	14	1 : 4	5	2 days
Horse*	70	8,400	5	3	1 : 2	5	2 days
Dog	9	2,700	15	3	1 : 4	5	2 days
Pig	250	40,000	30	3	1 : 5	15	3 days
Guinea-pig	0.5	13	1	2	1 : 2	20	2 h

Values are estimates after examination of the literature. They are based on the most extensive use of semen rather than the commonest methods in current use and are given only as an indication. In general, fewer spermatozoa are inseminated for semen stored at 5° C than samples deep frozen. Temperature and duration of semen storage refer to conditions that may be expected to give longest storage and ensure satisfactory pregnancy rates (about 60%) after artificial insemination.

* Several inseminations of semen that was deep frozen are usually required to obtain good conception rates; even so, results have been variable.

some of the glands. During ejaculation separate glands may, to varying degrees, secrete in order (for example, particularly so in the boar, dog and stallion but just detectably in the bull and man) so that an ejaculate may consist of one or several distinct fractions usually before and after a sperm rich fraction.

When possible, only the sperm rich fraction is collected for dilution, for seminal plasma is usually a poor medium for storing semen, and fractions of the semen of some animals gelatinize or cause coagulation. Thus, during ejaculation of the boar, for example, most of the spermatozoa are collected before the last, gelatinous fraction is emitted. But the coagulation of semen from rodents and some other animals remains a problem as it is not possible separately to collect the secretions of the glands that cause the formation of a hard rubbery mass (the seminal plug) from which spermatozoa cannot be separated. Surgical removal of the glands has been demonstrated[13], but it is time consuming and not generally practised.

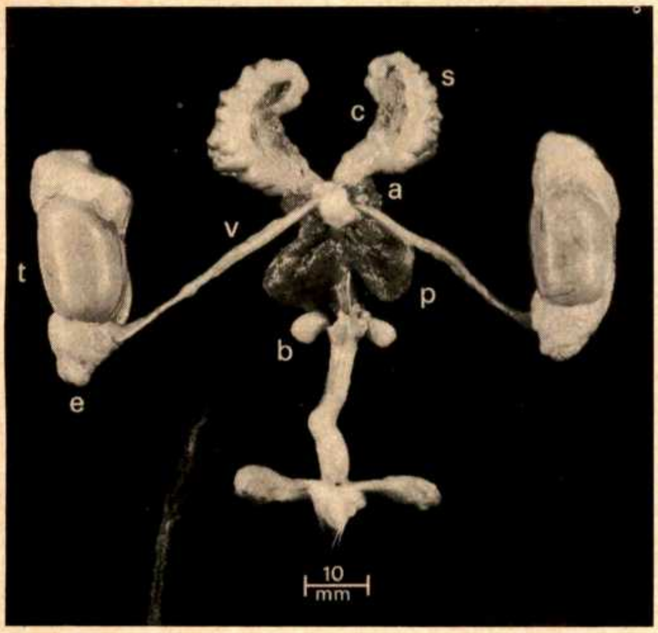

Fig. 1 Reproductive tract of male rat dissected to show the principal accessory organs. a, Ampullary glands; b, bulbourethral glands; c, coagulating glands; e, epididymidis; p, prostate glands; s, seminal vesicles; t, testis; v, vasa deferentia. Secretions from the glands and seminal vesicles constitute most of the seminal plasma. Secretions from the coagulating glands cause coagulation of semen to form a seminal plug.

The frequency with which semen can be collected from males varies greatly between species (Table 1). In the short term the reserves of spermatozoa in the epididymis can be exploited, but for continued collection the rate is limited by the production of spermatozoa in the testes. This varies between animals, according to the size of the testes and other factors. The bull and the ram have been estimated[14] to produce about 7×10^9 spermatozoa per day.

Evaluation and Preservation

A major difficulty in the application of artificial insemination and the storage of semen is the absence of a single or even a combination of criteria for predicting the fertility of a sample of semen. A relationship, of limited predictive value, between physical activity and fertility[15] is used for practical purposes and involves simple microscopic methods of estimating the number of living spermatozoa and their individual activity. The use of these methods has so far survived the development of numerous sophisticated devices involving photo-multipliers, a television scanner, cinematography and an impedance bridge.

Because spermatozoa are overcrowded in semen collected from most animals, samples must be diluted for storage. Diluents contain a metabolic substrate (usually a sugar) and electrolytes must be used in concentrations to account for the sensitivity of spermatozoa to changes in *p*H and osmotic pressure[16,17]. Milk[18] and egg yolk[19] or both are also included because of the protection afforded by their high molecular weight constituents against the damaging effects of cooling ("cold shock")[20] and dilution[16,21,22]. For frozen storage, glycerol[23] or dimethyl sulphoxide[24] must also be included to protect against the damage incurred during freezing or thawing. Further, antimicrobials[25,26] may be used to reduce the growth of organisms or the transmission of venereal diseases.

There have been numerous reports of poor results after the use of milk or egg yolk in diluents[27], and other natural products, such as tomato and coconut juice, have been used. None of the substitutes tested, however, is completely satisfactory either in the amount of protection afforded or the consistency of results. Unfortunately, much of the research into diluent composition has been of a very applied nature and there is still a need to define the specific chemical reagents that protect spermatozoa during various stages of processing[28].

There is a reduction in activity of spermatozoa as their temperature is decreased, and so the principal approach to long term preservation has been to store semen at low temperatures. Methods of preparing deep frozen semen are an extension of methods used to store semen at higher temperatures. A standard technique for deep freezing bull semen is to dilute freshly collected samples twenty to forty-fold with buffered egg yolk and cool to 5° C for one to three hours. Then it is further diluted 1 : 1 with a buffered glycerol solution (preferably containing a sugar[29]), stored for up to eighteen hours "to equilibrate", cooled to the freezing point of the eutectic mixture (about −12° C) at a rate of 1° C min^{-1}, cooled to −40° C at 3° C min^{-1}, and then transferred to refrigerators at the temperature of solid carbon dioxide (−79° C) or liquid nitrogen (−196° C). The type of diluent, rate of dilution and processing times are inter-related factors affecting the survival of spermatozoa so that, as may be expected, several quite different methods of freezing semen have been developed. These include two which may have economic advantages: freezing drops of diluted semen on dry ice[30] or cooling samples in liquid nitrogen vapour[31]. With the latter method samples may be contained in plastic straws that can be used as part of the inseminating pipette[32].

The detrimental effects of high dilution and "cold shock" vary in magnitude between species and are important factors limiting semen preservation. It is now possible to freeze bull semen without reducing the chance of pregnancy after a single insemination[33]. Encouraging results have also been obtained with deep frozen rabbit semen[34]. More than five-fold dilution, however, may reduce the fertility of ram semen, and cooling to 5° C causes a further reduction and only about 20% lambing can be expected after one insemination of deep frozen samples[35]. Poor or variable results have also been obtained with human, stallion and goat semen and there are no authentic reports of fertility of deep frozen boar or dog semen.

A reduction of viability and change in structure of spermatozoa[36,42] are usually associated with this reduction of fertility, and although these changes may not be highly indicative of fertility changes they are considered to indicate the importance of obtaining more viable spermatozoa after storage.

Detection of Oestrus

A major factor limiting the practice of artificial insemination is an incomplete knowledge of the reproductive physiology of the female. Because spermatozoa may have to spend a period in the female reproductive tract before acquiring the ability to fertilize[43,44] (that is, they have to capacitate) insemination must occur before ovulation. But because processed spermatozoa may have reduced viability their time in the female tract must be minimized.

The method used to detect ovulation depends on the reproductive pattern of the female. In some animals (rabbits, camelids and some mustelids) ovulation is induced by mating which may occur at any time during the breeding season. Ovulation can be induced in this type of animal by mating with a vasectomized male or injecting gonadotrophins.

In most animals, however, ovulation occurs spontaneously either near to or at the end of an oestrous (heat) period, or at about mid-cycle in menstruating animals. Injection of hormones can also induce ovulation in these animals, but only at certain times of the cycle. Indeed, except for man (and possibly some of the great apes) the female only accepts the male during oestrous periods. But because oestrus is a behavioural phenomenon and is not overtly displayed in many animals it is often difficult to detect. Methods of detecting oestrus include observation of behavioural activity of the female, the use of vasectomized males either carrying crayons that mark the female during mating or that leave a seminal plug in the vagina (for example, rodents) and daily inspection to detect cytological changes of the vagina or morphological changes of the external genitalia. Clearly it is advantageous to know and handle animals individually and this must be an important reason for the early success of artificial insemination of dairy cattle compared with animals (such as sheep), kept less intensively and in large flocks. For both technical and management reasons there is considerable demand for a method that will bring a large group of females into oestrus followed by ovulation at a precisely predetermined time. Some success along these lines has been obtained with cattle[46], sheep[47] and pigs[48] by administering a substance that inhibits ovulation (usually a progestagen) to the flock for a certain period and withdrawing treatment at a predetermined time. Oestrus subsequently occurs over several days, and the time of ovulation can be controlled more precisely by injection of a gonadotrophin. Unfortunately, this method has been of limited value because conception rates are low at the first oestrus after withdrawal and synchronization is poor at the next oestrus.

When ovulation time has proved difficult to predict, good fertility has often been obtained by inseminating the female at intervals near the expected time of ovulation. Insemination may also be done during several consecutive oestrus periods. Reports of reasonable to good pregnancy rates after artificial insemination of deep frozen human[49], stallion[50], goat[51] and ram[52] semen can probably be explained largely as a consequence of repeated inseminations of the female. But this "shot-gun" approach really evades the problems and should be considered an intermediate measure during the development of suitable insemination techniques. The unstated use of these methods is probably a reason for inconsistent reports in the literature on the fertility of stored semen.

Method of Insemination

Cows can be inseminated artificially by guiding a pipette, loaded with spermatozoa in 0.5–1.0 ml. of fluid, through the lumen of the vagina and cervix into the uterus and expelling the contents into the uterine horns (Fig. 2). Methods of preparing and inseminating semen, however, must be varied according to the structure of the female reproductive tract.

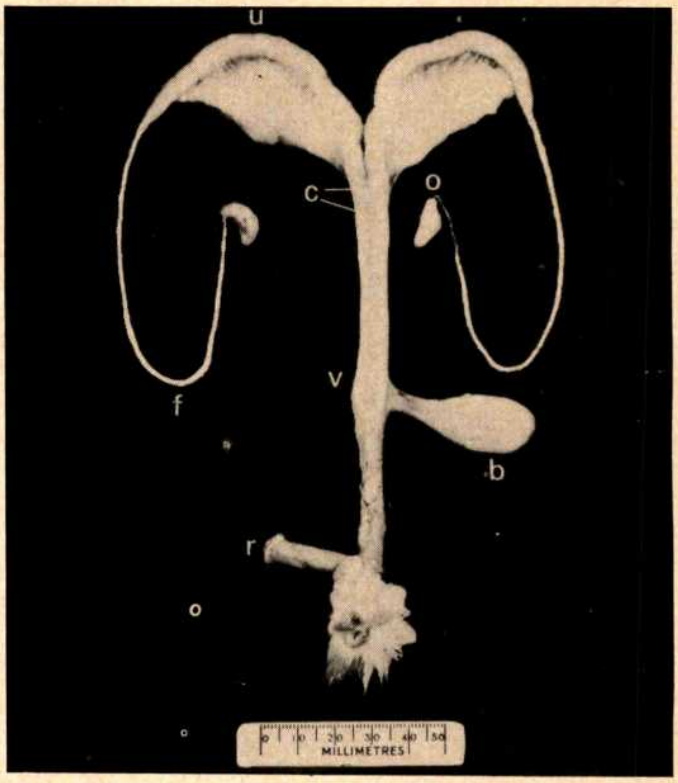

Fig. 2 Reproductive tract of female rabbit dissected to show: b, bladder; c, cervices; f, fallopian tube; o, ovary; r, rectum; u, uterine horn; v, vagina. The vagina of the rabbit is particularly long and is joined to the separated uterine horns by two cervical canals. Does are artificially inseminated by depositing semen samples at the anterior end of the vagina so that spermatozoa may penetrate both cervices.

Embryologically the tract develops from the paired Müllerian ducts, which differ among animals in the amount of development and fusion of the vaginae, cervical canals and uteri (Fig. 2); from the duckbilled platypus in which the full length of the tract is paired, to humans in which the tract is singular, proximal to the fallopian tubes. Thus, depending on species, semen must be deposited into one or two vaginae, cervices or uterine horns to ensure that spermatozoa reach both fallopian tubes. Further, as the wall of the cervix of some animals (such as the ewe) is deeply folded it limits penetration of the insemination pipette.

The number of spermatozoa (Fig. 3) and the volume of fluid inseminated are also important factors. At least 50 ml. of fluid must be used to inseminate a sow but less than 0.2 ml. is needed for a ewe. A factor which limits the dilution of ram semen is the difficulty of inseminating fluid into the cervix of the ewe[35,53], and the problem can be avoided by concentrating the semen before insemination by centrifuging and removing excess fluid.

The importance of the male has been too readily overlooked by many technologists practising artificial insemination. The seminal plug formed by the semen of many rodents and some other animals may not be necessary for good fertility after natural mating, but it could be useful after artificial insemination to ensure that spermatozoa are not lost from

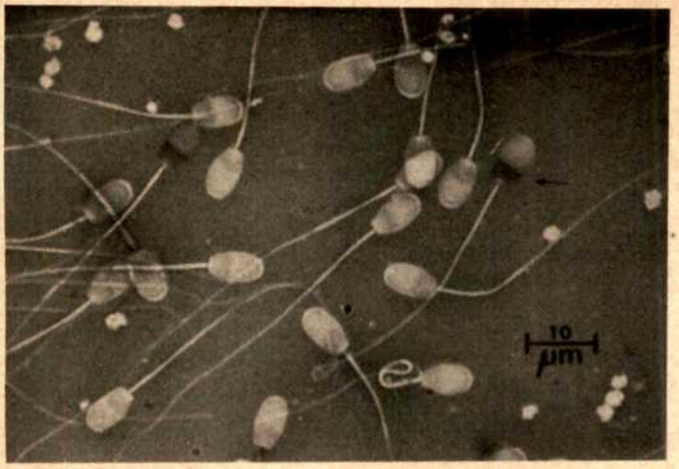

Fig. 3 Photomicrograph of an eosin–nigrosin smear of ram semen. The staining reaction of eosin is commonly used in semen evaluation; spermatozoa stained with the dye (arrow) are considered "dead".

the female reproductive tract. Indeed, although human semen does not form a plug (but does gelatinize for a short time) it is recommended[49] that a cervical cap be used when inseminating women.

It has already been mentioned that coitus induces ovulation in some animals and must be accounted for during a programme of artificial insemination. Furthermore, when inseminating the laboratory rat or mouse the stimulation of the cervix by the male during coitus must also be substituted to ensure that a functional corpus luteum is formed and that the uterus is prepared for implantation of the embryo. Also, the effect of mating on the release of oxytocin from the posterior pituitary and the importance of this and the oxytocic substance in semen on transport of spermatozoa through the female reproductive tract are poorly understood. Certainly it has been shown that post-insemination coitus is beneficial in sheep[54].

The presence of the male, without any contact, may also be important[55], for as well as affecting behavioural activity of several animals, pheromones, by chemical communication, may be necessary to maintain pregnancy and cyclic activity of some rodents.

Future of Artificial Insemination

The future application of artificial insemination depends largely on improvements in methods of detecting oestrus and ovulation and of semen collection, evaluation, preservation and insemination. Many of these will undoubtedly come as by-products of an increased knowledge of the physiology of reproduction. Nevertheless, the development of such methods as electro-ejaculation and the use of glycerol indicate the value of research orientated towards application.

The future of artificial insemination also depends on other technological developments. Those that would complement the technique and increase its use are development of methods to separate spermatozoa according to fertilizing capacity, the possession of sex determining chromosomes or the absence of abnormal chromosomes or chromosomes carrying "lethal" genes. Alternatively, if it proves practicable to transfer ova or embryos to foster mothers and to develop suitable methods of superovulating females, fertilizing ova *in vitro* and deep freezing ova or embryos, their use might, to some degree, supersede that of artificial insemination.

At present there is a considerable demand to improve and expand the application of artificial insemination of domestic animals. Indeed, improvements of economic conditions in underdeveloped countries alone will be associated with its use to up-grade farm animals. Its increased use with man seems probable at least for therapeutic reasons, as in cases of oligospermia. And changes in world attitude may ensure that semen preservation and artificial insemination will play a part in the preservation of wild animals. But regardless of future developments of countries and techniques, artificial insemination will be used for some time as a research tool.

I thank Dr I. W. Rowlands for helpful advice and criticism and Mr T. J. Dennett for the photography.

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Structure and Evolution of the Kenya Rift Valley

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Geological evidence makes possible a reconstruction of events since Miocene times, with about 10 km of crustal separation and the pressure beneath the central rift of an upward intrusion from the mantle.

THE Kenya rift valley is one of the better known parts of the eastern rift system of Africa[1], which extends from north Tanzania through Kenya and Ethiopia to join the Red Sea and Gulf of Aden rifts at the Afar triple junction (Fig. 1). The axial Sheba ridge of the Gulf of Aden[2] is continuous with the Carlsberg ridge of the NW Indian Ocean[3], so that the eastern rift of Africa is a continental extension of the world rift system—an interpretation which is reinforced by studies of the seismicity[4] and plate tectonics[5] of the Afro-Arabian region. The purpose of this article is to summarize modern geological knowledge of the Kenya rift and to reconcile this with crustal models and kinematic concepts derived primarily from geophysical data.

Epeirogenic Movements

The Kenya domal uplift is a local culmination on the eastern rim of the East African plateau. It is elliptical in plan and about 1,000 km wide. Studies of the shape and height of well preserved erosion surfaces of Miocene and late Pliocene ages provide evidence for three main phases of epeirogeny and crustal flexuring, consisting of periodic up-arching of central Kenya and local downwarping of the coastal zone[6]. Early Miocene monoclinal upwarping of the Kenya–Uganda border area was accompanied by downflexing of the Turkana depression and local faulting[7]. A broad domal uplift of central Kenya of about 300 m in the late Miocene was succeeded by a major uplift of 1,400 m during late Pliocene to mid-Pleistocene times[6]. Fig. 2 shows isobases of the sub-Miocene erosion surface and indicates the sum of uplifts since the mid-Tertiary, which reached maxima of 1,700 m.

Rift Fault Pattern

The major faults define a complex graben (the Gregory rift[8]) which trends meridionally along the major axis of the uplift (Fig. 2). North and south of the Gregory rift, in Turkana and north Tanzania, the periclinal ends of the uplifted area are broad transverse depressions traversed by splay-faults. The major faults branching from the Gregory rift in these areas are antithetic in character and almost always downthrow eastwards.

The Gregory rift is in the central part of the Kenya rift zone, and is a complex graben 60–70 km wide bounded by major normal faults arranged *en echelon*. Broad step-fault platforms occur locally at each side of the graben, and between the hinge faults *en echelon* there are sloping ramps descending from the flanking plateau to the rift floor. The fault escarpments are well preserved and range up to 2,000 m in height in the central sector. The thickness of volcanics of the plateau (up to 2,000 m) and the still greater thickness of the volcanic and sedimentary fill in the rift floor which is inferred suggest that the throws of the major faults may reach 3,000–4,000 m. The floor of the Gregory graben, including the step-fault platforms and ramps, are cut by dense swarms of young, sub-parallel minor faults[9–11].

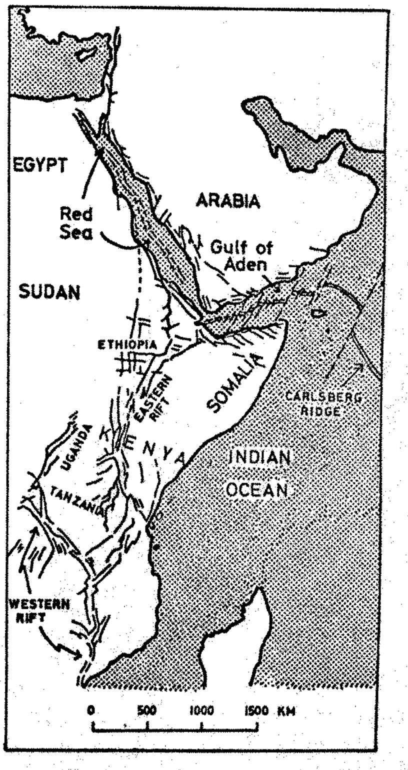

Fig. 1 Structural pattern of the Afro-Arabian rift system, showing the eastern and western rifts of Africa.

Notable features of the fault pattern are the element of symmetry about the minor (E–W) axis of the uplift and the location of the main rift on the crest and major axis. This bears out the view that there was a genetic connexion between epeirogenic upwarping and rift faulting.

Evolution of the Kenya Rift

The oldest recognizable rift structures are the dissected monoclinal flexure now represented by the Uganda escarpment[7], and the related Turkwel fault (Fig. 3). They are mid-Tertiary, for they immediately pre-date the Miocene volcanics of the Turkana depression. An upwarped region along the Kenya–Uganda border was the site of lower to middle Miocene nephelinitic central volcanism[12], and the complementary Turkana depression was partly filled by contemporaneous flood basalts[7,13]. In late Miocene times the central rift area was slightly uplifted, and was the site of massive fissure phonolite eruptions[13].

The first extensive rift faults developed early in the Pliocene at the culmination of the Miocene uplift phase, producing a meridional asymmetrical trough faulted mainly on its western side (Fig. 4). There was relatively minor phonolite and trachyte volcanism in the floor of the central part of this trough in the mid-Pliocene, but this was followed by much more voluminous basalt eruptions along nearly the whole length of the trough together with the formation of the dominantly basaltic Aberdare central volcanic range[13].

In late Pliocene times, massive eruptions of trachytic ignimbrites began in the Naivasha sector of the rift floor[14], locally filling the rift and overflowing its flanks (Fig. 5). At about the same time, the last and major uplift of the marginal plateaux began, accompanied by the first of several phases of graben faulting, which created the outline of the Gregory rift. The developing graben was partly filled by lower to middle Pleistocene flood trachytes[13,16]. Further local rejuvenations of the main graben and step faults continued until mid-Pleistocene times, deepening the Lake Naivasha and Lake Natron sectors. At the same time, the graben floor was shattered by swarms of closely spaced minor faults[9–11], which in some places reach densities of 2 to 3 faults per km (Fig. 6).

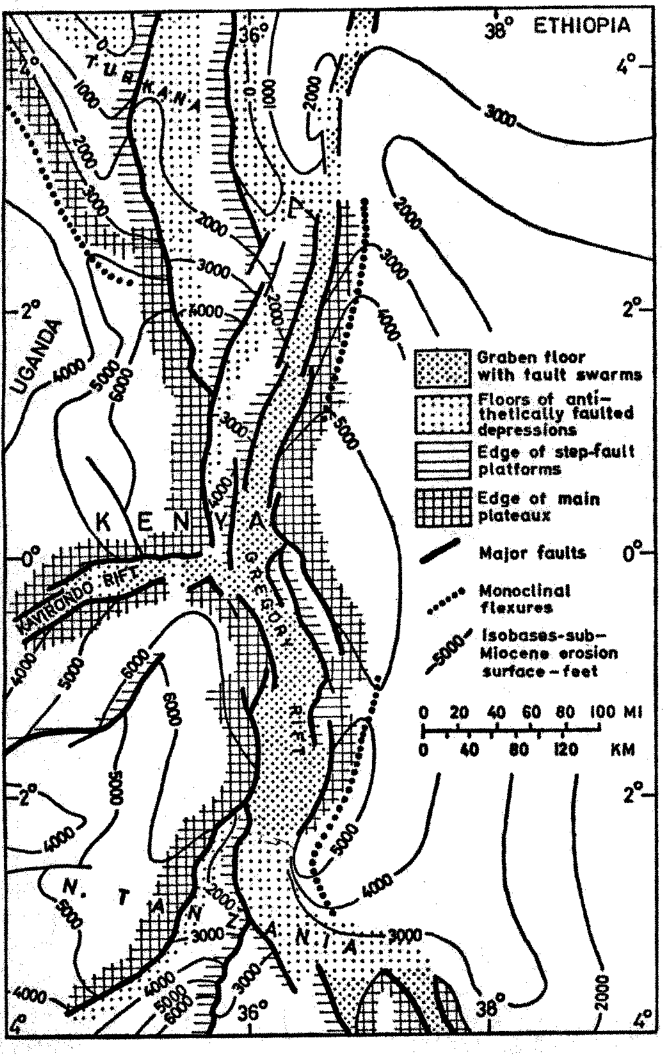

Fig. 2 Structure of the Kenya rift zone. The contours indicate the amount of crustal uplift since the mid-Tertiary in feet.

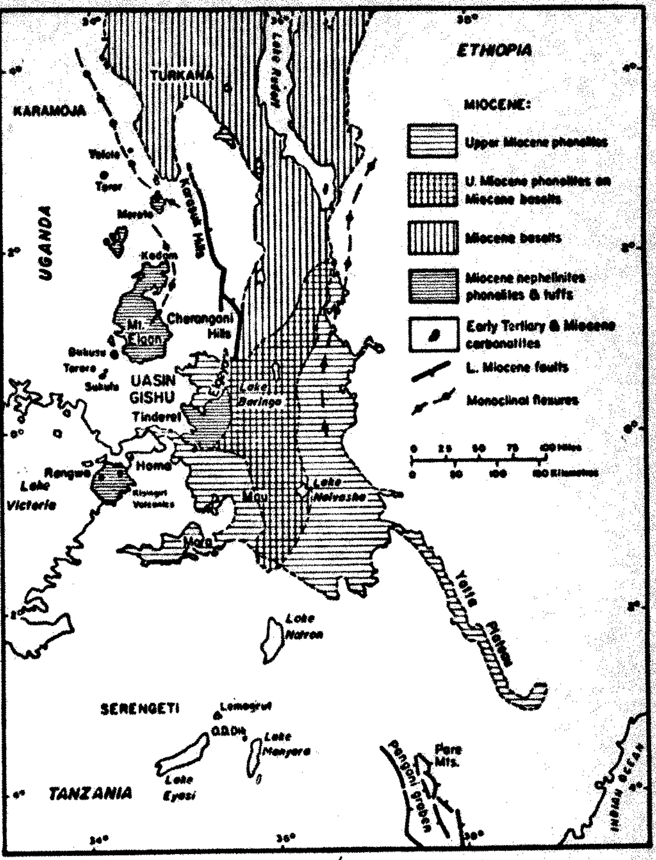

Fig. 3 Miocene volcanism and faulting in Kenya.

In the later Quaternary, trachyte, basalt-trachyte and phonolite caldera volcanoes[15] built up axially in the floor of the inner graben, while in areas well to the east of the rift there were extensive basalt eruptions in three main areas forming linear multicentre volcanic chains[16] (Fig. 6).

Thus in the Miocene, the Kenya rift passed through a period of broad crustal flexing and local faulting accompanied by basic volcanism, succeeded in the late Miocene by voluminous flood phonolite eruptions. The first faulting to affect the whole length of the rift took place in the early Pliocene, creating an asymmetrical graben. This was followed by dominantly basaltic volcanism in the floor of the rift depression, but towards the end of the Pliocene the last and major uplift of the plateaux began and was accompanied by massive trachytic volcanism and phases of graben faulting.

Kinematics of Rifting

The formation of the Gregory rift has been explained in a variety of ways—as a result of crustal doming[17]; of crustal stretching and thinning[18]; the subsidence of a block as a result of isostatic forces[19]; and as a zone of crustal rupture and injection of igneous rocks[5,22]. The depth of the graben is too great for the doming or isostatic models to be adequate[20]. If the fault planes have mean dips of 63°, there must have been at least 5 km of crustal extension to account for the observed structures. Since there are likely to be many concealed faults under the graben floor, the total crustal extension inferred on structural grounds could range up to 10 km, and this is much more than could result from crustal arching[21], showing that the faulting cannot have been the result of doming alone,

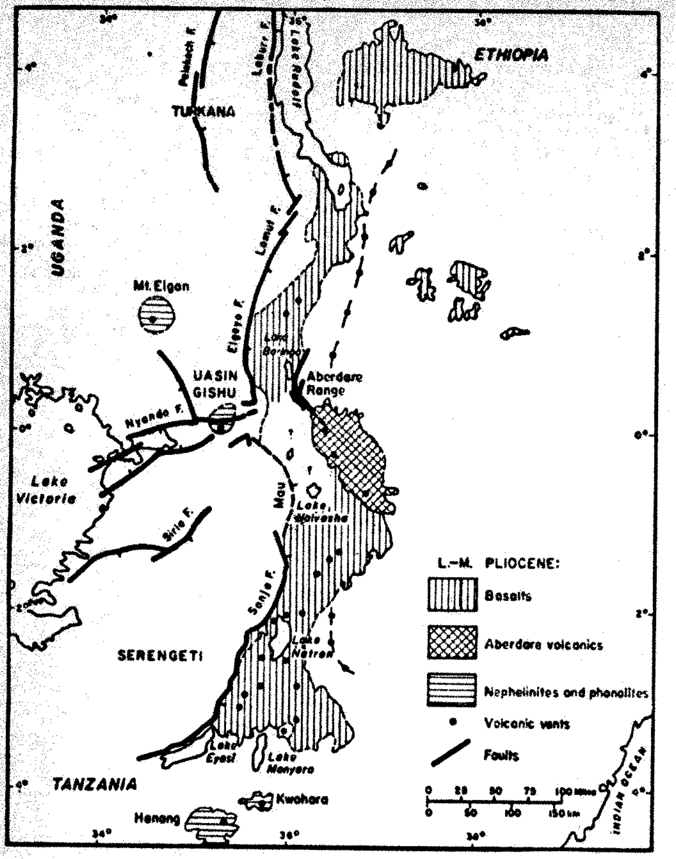

Fig. 4 Lower to middle Pliocene volcanism and faulting in Kenya.

so that both doming and faulting must be related results of some sub-crustal process.

In a model involving crustal disruption and separation[5,24], the maximum amount of crustal separation could not have been more than the 20–30 km width of the inner graben of the Gregory rift, for the step fault platforms bordering the inner graben locally expose Pre-Cambrian rocks and down-faulted formations of the adjacent plateaux. At the north and south extremities of the Kenya domal uplift, in southern Ethiopia and north Tanzania, Pre-Cambrian rocks outcrop across the whole width of the rift zone, showing that there can have been only about 3 km of crustal extension in those areas as a result of normal faulting. Thus the geological data will allow between 5 and 25 km of crustal extension (or separation) in the central sector of the Gregory rift but not more than about 3 km at its extremities. The absence of cross-rift faults of transform type that could account for large variations of crustal extension along the rift zone suggests that the crustal extension across the central rift was closer to 5 km than to 25 km.

There are sufficient gravity measurements[22] in the area of the central Gregory rift to allow a Bouguer gravity anomaly profile to be drawn (Fig. 7*a*). The usual specific gravity of 2.67 has been used for the Bouguer reduction to sea level, with the result that the structural complexity and the existence of some thousands of metres of low density volcanics on the flanks and in the floor of the rift exert a strong influence on the shape of the profile. In a computed[23] two-dimensional model of crustal structure (Fig. 7*b*) we have included low density zones (specific gravities 2.0 and 2.2) on each side of the rift valley to minimize the insufficient Bouguer compensation resulting from the presence of these low density volcanics. The computed Bouguer anomaly of the model agrees with the observed profile within reasonable limits (Fig. 7*a*). To explain the positive peak in the profile, the model has to contain an intra-crustal body with a positive specific gravity contrast of 0.15, the top of which is 10 km wide and reaches through the crust to 1,500 m below sea level under the inner graben of the Gregory rift. This body (specific gravity 3.05) could represent a wedge shaped basic intrusive mass. Other interpretations of the gravity data yield similar crustal models[22,24], but with wider (16–28 km) dense bodies beneath the rift floor.

Support for the presence of a zone of low density upper mantle beneath the rift comes from interpretations of Bouguer gravity anomaly profiles across the East African plateau[18,25] and from observation of P wave delays (personal communication from E. B. Rodrigues), S wave attenuation[26] and studies of seismic wave transfer spectra[27] for paths along the rift to the Nairobi WWSS station by comparison with paths of other azimuth. The presence of a relatively high density body within the crust beneath the rift valley is also suggested by preliminary results of seismic refraction work, which indicates the presence of a body with a seismic velocity of 6.5 km/s less than 20 km beneath the north-central part of the Kenya rift[28]. Similar conclusions have been drawn from earthquake studies of the western rift[29].

The crustal model (Fig. 7*b*) suggests there has been about 10 km of crustal separation under the central part of the Gregory graben, together with the injection of basic igneous rocks derived from a presumably hot and partly molten zone of low density in the upper mantle. The centre of the basic intrusive body on the profile lies just south of Menengai crater (Fig. 6), and the gravity measurements show that it trends NNW and SSE along the floor of the inner graben. The rift floor in the zone above the basic intrusive body consists of late Pliocene ignimbrites overlain by lower Pleistocene trachyte lavas, and there is nothing to distinguish its structure from the rest of the rift floor, nor is it characterized by any alignment of volcanic centres[10]. There are no quater-

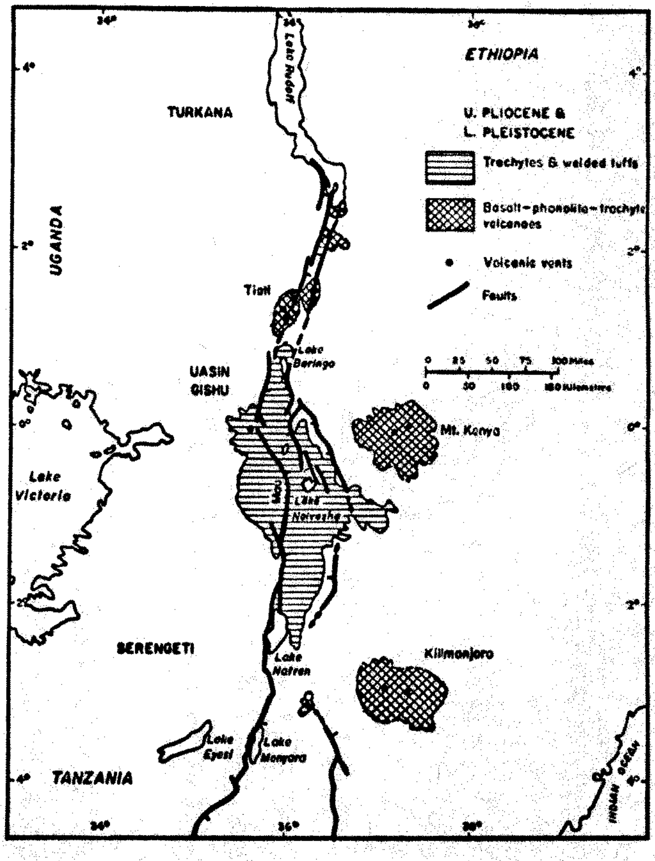

Fig. 5 Upper Pliocene and lower Pleistocene volcanism and faulting in Kenya.

nary basalt volcanoes in this area, and they are extremely rare throughout the Gregory rift[16].

Since it is most probable that basic igneous injection into and through the crust would be accompanied by basaltic volcanism and structural effects, it is probable that the period of crustal separation and basic igneous injection took place in pre-upper Pliocene times, perhaps at the time of the extensive mid-Pliocene basalt eruptions that flooded much of the rift floor (Fig. 4) or during the Miocene basaltic volcanism (Fig. 3). The massive late Pliocene and Quaternary sialic volcanism of the central Gregory rift, which produced about 100,000 km³ of trachytic eruptives[16], evidently succeeded the period of crustal separation and concealed its volcanic and tectonic effects. What kind of petrogenetic process produced this large volume of trachytic eruptives is uncertain[30], but it is possible that crustal disruption and basic igneous injection was followed by anatexis of fenitized sialic rocks[12] or by some form of crustal assimilation[31].

The 10 km of crustal separation beneath the central Kenya rift suggested by the gravity data is much less than the 30 km of crustal separation suggested by plate tectonics[5]. Recent modifications[32,33] to the plate tectonics scheme, which involve bringing the Arabia–Nubia and Arabia–Somalia rotation poles closer together, does, however, imply a much reduced crustal extension across the eastern rift, closer to the 10 km indicated by the gravity data.

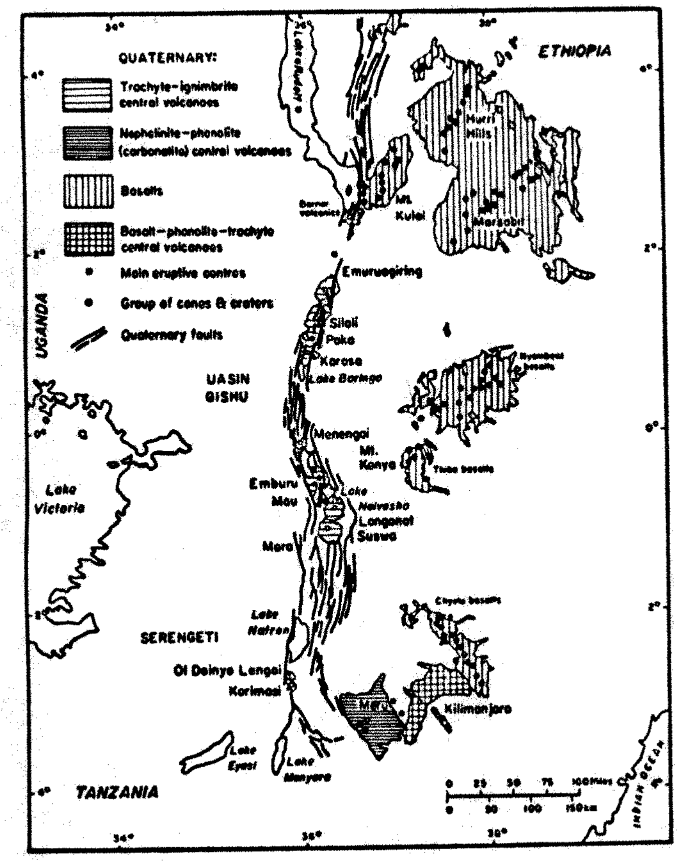

Fig. 6 Late Quaternary volcanism and faulting in Kenya.

In summary, it seems that the formation of the Kenya rift valley is the result of phases of epeirogenic uplift, volcanism and faulting since lower Miocene times. The underlying process seems to have been the rise of geotherms in the upper mantle, leading to partial melting and regional up-doming of the crust. The main Miocene and late Pliocene–early Pleistocene taphrogenic episodes began with basic volcanism accompanied by crustal disruption and magmatic injection, and ended with regional uplifts and intermediate and silicic volcanism, during and after which the main graben faulting occurred. The later and most important of these episodes was accompanied by the eruption of such large volumes of trachytic ignimbrites that it is reasonable to suppose that part at least of the collapse of the floor of the Gregory rift resulted from the rapid eruption of lava. The surface geology of the floor of the central Kenya rift does not show features related to 10 km of crustal separation, but since the pre-Quaternary structural history of the inner graben is largely conjectural, this means that the crustal separation must have taken place mostly in the Tertiary, its effects being subsequently obscured by later volcanics and sediments which partly filled the graben.

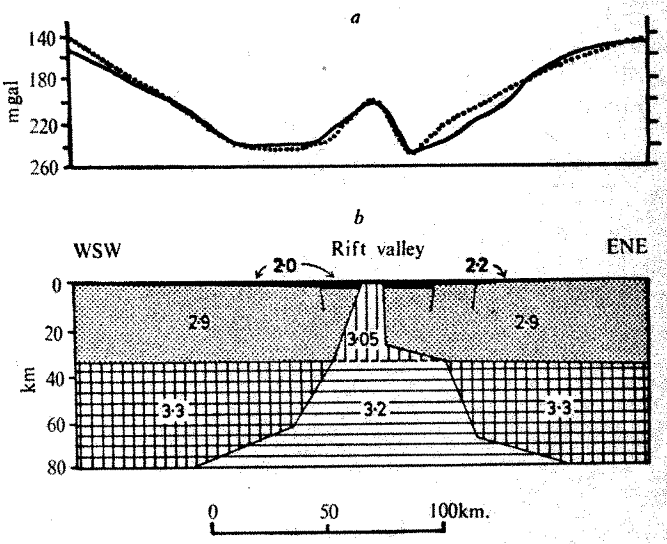

Fig. 7 *a*, Bouguer gravity profile across the Gregory rift, orientated ENE–WSW, and crossing the central rift just south of Menengai (see Fig. 6). The continuous line is the observed Bouguer gravity anomaly and the dotted line is the computed anomaly for the crustal model shown in *b*.

Although the Kenya rift is linked to the world rift system, and the underlying mantle processes are probably similar throughout the system[34], it should not be regarded as a model for oceanic ridge-rifts nor even as a typical example of the first stage of continental break-up. The mean spreading rate of the Kenya rift is not more than 0.5 mm a year compared with 1–2 cm a year of the Red Sea and Gulf of Aden and 2–10 cm a year for the mature mid-ocean ridges[35]. Hence the Kenya rift is best regarded as part of a weak branch of the Carlsbad–Sheba ridge–Red Sea axial trough spreading axis, characterized by exceedingly slow rates of crustal extension and by long-continued interaction between crust and thermally activated mantle.

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Parameter Sensitivity as a Criterion for Evaluating and Comparing the Performance of Biochemical Systems

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Parameter sensitivity is a theoretical criterion that can be used in the quantitative evaluation and comparison of different biochemical systems that regulate, for example, the supply of end product.

REPRESSION of enzyme synthesis and inhibition of enzyme activity by the end product of a biosynthetic sequence, sometimes operating in conjunction, serve to regulate the supply of the end product[1]. The energy conserved in these ways by producing only the necessary complement of enzymes and intermediate metabolites is also believed to be a significant contribution to the efficiency of the organism. Although these ideas have been apparent since the initial discoveries in this area, there have been few attempts to establish criteria by which the effectiveness of different systems in performing these functions can be evaluated and compared. This seems to be true for biochemical systems in general. Although there are numerous physical and chemical techniques for characterizing the components of a biochemical system, there are relatively few quantitative measures for those specific properties and behaviour patterns, such as regulation, that emerge at the level of organized networks of enzyme-catalysed reactions.

One quantitative measure for the performance of a regulated biosynthetic pathway is provided by the relative growth rates of two strains of bacteria that are presumed to be identical, except for a difference in the control of a pathway. This criterion has been useful in investigating the evolutionary advantage conferred on an organism by biosynthetic pathways controlled by repression[2] or by end product inhibition[3]. This measurement actually determines "selective advantage" and as such it is a complex mixture of effects related to both the organism and its environment. Indeed, as these studies have shown[1,2], the ratio of the growth rates of the two organisms is strongly dependent on the type of medium used to support their growth. From this we conclude that the rate of growth is related only in a rather non-specific way to the function of the particular control system under consideration. Furthermore, unless special precautions are taken to ensure that the pathway in question is rate-limiting for growth, this measurement may actually reflect secondary changes in the total metabolism of the cell rather than changes in the primary function of the modified control system. These ambiguities indicate that a more specific criterion of performance is needed for such biochemical systems.

Ideally, we should like criteria for measuring the effectiveness of a biochemical control system to meet the following requirements. First, they should be quantitative. This is for greater objectivity and for distinguishing not only a completely functional from a completely nonfunctional system, but a spectrum of systems functioning with different efficiencies. Second, they should be relevant. By this I mean the criteria must be directly related to the particular function of the system in question, thus avoiding confusion with irrelevant or secondary phenomena. Finally, they should be invariant. They should represent an intrinsic property of the system that relates changes in the system or its environment to the resulting changes in the behaviour or response of the system; and such relationships should be unaffected by the particular magnitude of the change or the particular way in which the original change was produced.

To facilitate the remaining discussion I shall consider the didactic system shown schematically in Fig. 1; it may be thought of as a biosynthetic pathway consisting of a single enzyme subject to repression at the transcription level with the end product as the co-repressor. One of the primary functions of such a control system is presumably to maintain a relatively constant supply of the end product in spite of changes in the system itself or in its environment. In this communication the criterion of parameter sensitivity is defined as relevant for assessing the ability of such control systems to "buffer" the end product concentration against changes internal to the system itself. This aspect of biochemical feedback control is just as important but less often appreciated than its ability to counteract changes in the environment. An analysis of the effects of environmental changes is presented elsewhere (my unpublished work).

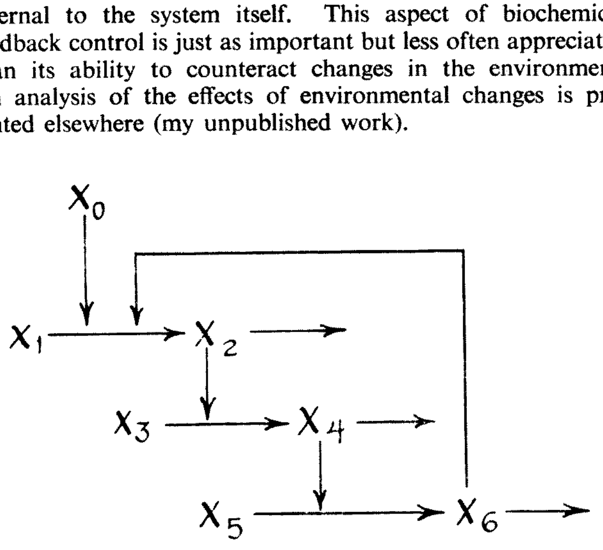

Fig. 1 A schematic representation of a biosynthetic pathway consisting of a single enzyme whose synthesis is subject to repression at the transcription level and whose end product serves as the co-repressor. X_0, Structural gene for the enzyme; X_1, weighted sum of the nucleotide pools; X_2, specific messenger-RNA; X_3, weighted sum of the amino-acid pools; X_4, enzyme; X_5, substrate; and X_6, end product. The transfer of material from one pool to another is represented by an arrow from the symbol denoting the original pool to the symbol denoting the final pool (for simplicity the explicit representation of the final pool is in some instances omitted). A modification of this transfer by a third substance is represented by an arrow from the symbol denoting the modifier to the middle of the arrow representing the transfer. All the modifications in this diagram are positive except for the modification of the $X_1 \rightarrow X_2$ reaction by X_6, which is negative since X_6 acts in conjunction with other molecules to repress this conversion. Those additional modifiers and/or "cofactors" that are not of primary concern here have been omitted from the diagram.

The following definition of parameter sensitivity meets these requirements and avoids the difficulties encountered in measuring the effectiveness of a biochemical control system that I have mentioned. If a parameter is a property of the system that is normally a fixed quantity, and is in different systems or in different environments, parameters can assume different values—for example, in a simple enzyme catalysed reaction, the Michaelis constant K_m would be a parameter of the system, whereas the concentration of the substrate would be a variable—in the steady state, the relative variation (or percentage change) in some property X, related to the system function in question, with respect to the relative variation of a parameter α, is defined as the parameter sensitivity of X with respect to α, that is,

$$S_{x\alpha} = \frac{\delta X}{\delta \alpha} \quad \frac{\alpha}{X} \tag{1}$$

This is a general definition and can therefore be applied to many different functions and parameters in a wide variety of systems. In experimental practice, the parameter sensitivity would be measured using finite differences, and the expression in (1) would be approximated as

$$S_{x\alpha} = \frac{X_2 - X_1}{X_1} \quad \frac{\alpha_1}{\alpha_2 - \alpha_1} \tag{2}$$

where the subscripts 1 and 2 refer to values before and after a change in the parameter value respectively. In reference to Fig. 1, we shall consider the concentration of the end product as a property directly related to the function of the system, as this function is described in the previous paragraph; the molecular activity or turn-over number of the enzyme is considered an intrinsic or characteristic parameter of the system. Thus the parameter sensitivity of the end product concentration, X_6, will be examined in response to changes in the molecular activity of the enzyme, α.

One might imagine this change in molecular activity to be produced in any of a number of ways. We shall assume that a mutation in that portion of the genome coding for the biosynthetic enzyme has caused a partial loss of activity in the enzyme molecules. Other things being equal, the effect of such a change would be a reduction in the concentration of the end product, and consequently in the rate at which it is used up, until the rate of utilization balanced the new, reduced rate of synthesis. This reduction in the concentration of the end product, however, would tend to derepress the synthesis of new enzyme molecules, which in turn would increase the rate of synthesis of the end product back toward its normal level. Thus, the activity of the enzymes present is decreased, but the quantity of the enzyme is increased by derepression. The net effect is but a slight decrease in the supply of the end product. These qualitative results are fairly self-evident. The important point for this discussion is that the more effective the compensation by derepression, the smaller the resulting change in the concentration of the end product for a given change in the molecular activity and, therefore, the lower the parameter sensitivity. Thus, parameter sensitivity in this example measures the effectiveness of feedback repression in compensating for internal changes.

A numerical value for the parameter sensitivity in this case could be obtained by measuring the molecular activity of the mutant and wild type enzymes, as well as the endogenous concentration of the end product in steady state for both the mutant and wild type organism. Although we are not primarily concerned here with details of the experimental measurements, it could be pointed out that it might be difficult to determine the conditions in which the molecular activity should be measured *in vitro* so as to mimic the value existing in the cell. One might hope, however, that these values would differ by the same percentage for both the mutant and the wild type enzyme. If this were so, then the calculation of percentage variation due to mutation would be unaffected by the changes in each of the individual measurements. A more detailed analysis of parameter sensitivity shows that alternatively one may utilize the expression $-(\delta X_6/\delta X_4)(X_4/X_6)$ as a close approximation to the true value when the parameter sensitivity is slight. In this method one would measure differences in the amount of wild type and mutant enzyme rather than differences in their molecular activity. Changes in the concentration of the end product could be measured by a number of chemical, enzymatic, or radioisotopic techniques.

Suppose that in the mutant organism there is a 10% decrease in molecular activity and a 1% decrease in the end product concentration; this parameter sensitivity of the control system would have a value of 0.10. This number is a constant independent of the magnitudes of the changes over some appropriate range and it is therefore characteristic of the particular system under consideration. The consistency of this relation is due in part to the fact that one is dealing with a ratio of changes. Thus, one would get the same result if a 20% decrease in molecular activity were to cause a 2% decrease in the end product concentration. Furthermore, the use of percentage variation tends to eliminate the differences in absolute magnitude that might be produced by different environmental conditions. The constancy of this relation also makes it useful for predictive purposes. Once this parameter sensitivity of the system has been determined with one type of mutation, one can calculate from observed changes in the end product concentration what the changes in molecular activity must be for a different mutation in the same cistron. Conversely, from a knowledge of the changes in molecular activity, one can predict what the changes in the end product concentration will be.

It should be emphasized that this important property of the intact system can in no way be obtained solely from experiments with the individual components or reactions of the system. Biochemical feedback regulation and the parameter sensitivities in such systems are properties that emerge only at the level of integrated networks of reactions. As more detailed analysis shows (my unpublished work), however, parameter sensitivity can be determined from a knowledge of the individual components of the system when this knowledge is coupled with an appropriate method of systems analysis or, alternatively, from direct physiological measurements in the intact system, as I have indicated.

The effect of change in other parameters could be investigated, and the mechanism for introducing a change in parameter value need not be genetic mutation. One could also examine other properties of the system besides the supply of the end product, but the choice in each instance will be guided by the hypothesis concerning the function of the system. The concept of parameter sensitivity is not restricted in any way to the example used here for illustration. For example, this concept has been used successfully in a comparative analysis of biosynthetic pathways subject to feedback control by inhibition at the molecular level (my unpublished work). Thus the criterion of sensitivity provides a useful quantitative tool for evaluating and comparing the effectiveness of biochemical systems.

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Variability of X-ray Emission from M87

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New rocket observations of this galaxy, distinguished by an optical jet 1,500 parsec long, suggest a variable X-ray emission probably linked with inhomogeneities in the jet.

WE first reported[1] X-ray emission from the direction of M87 in 1965 (ref. 1) and several measurements[2-4] have subsequently been made. The position of the X-ray source has been fixed in declination to ±0.1 degree by a fan beam scan. The new observation reported in this article places the source inside an error box of 0·1 square degrees that includes M87. Both the flux and the shape of the X-ray spectrum in the present observation differ markedly from previous observations, implying a high degree of variability. Evidence for X-ray emission from the quasar 3C 273 was also obtained, although with much lower statistical significance than for M87.

Observation of M87

On March 28, 1969, observations were carried out with two proportional counters aboard an Aerobee-Hi rocket which was launched from White Sands Missile Range. Each counter was equipped with a multiple slit collimator exposing a field of view of 1° × 8°. The slit orientations were crossed as shown in Fig. 1. The window material was 0.00015 inch "Mylar" coated with 70 Å of evaporated nichrome and the gas filling was a mixture of 90% argon and 10% methane at a pressure of 16 pounds per square inch. The unobscured window area of each counter was 254 square centimetres. A plastic anticoincidence shield surrounded each counter on five sides. All of the available observing time was devoted to a slow scan across 3C 273 and M87 as shown in Fig. 1 and the direction of pointing was determined from star field photographs taken every 5 s.

To produce the scanned data plotted in Figs. 2 and 3 the individual count versus time were matched at the instant of crossing of each source and the counts from both counters were summed. M87 was clearly detected with large signal-to-noise ratio by each counter; 3C 273 produced a signal equivalent to three standard deviations (3σ) only in the summed scans of both counters. By means of pulse height analysis, the spectrum of M87 was derived as shown in Fig. 4. A similar observation by Adams *et al.* nine months earlier indicated a much harder spectrum and a flux in the 1–10 keV range roughly an order of magnitude greater. There is no evidence of self absorption in the source. Table 1 lists all the observations reported for M87 up to the time of the last NRL flight, and it is clear that the range of flux values seems to be several times as great as any possible systematic errors in the individual measurements.

Table 1 Observations of X-rays from M87

Observer	Flux (erg cm^{-2} s^{-1})	Energy range (keV)
NRL (1965)[1]	$(2\pm1)\times10^{-9}$	1–10
NRL (1967)[2]	$(8.7\pm2)\times10^{-10}$	1–10
MIT (1967)[3]	$(5\pm2)\times10^{-10}$	1.5–6
Leicester (1968)[4]	$(1.5\pm0.3)\times10^{-9}$	1·5–5
NRL (1969)	$(1.9\pm0.2)\times10^{-10}$	0.8–4

A number of balloon flights have been made in attempts to observe M87 at energies above 25 keV. Haymes *et al.* claimed[5] a significant result in 1967 at about 40 keV, which falls on the extrapolation of the radio spectrum with a single power law index of −0.7 extending all the way from radio through optical to the X-ray wavelengths. Two attempts by the UCSD group[6] in February 1967 and in June 1968 did not, however, detect the source and gave upper limits significantly below that claimed by Haymes *et al.* Overbeck and Tannenbaum[7] in 1968 and McClintock *et al.*[8] in 1969 estab-

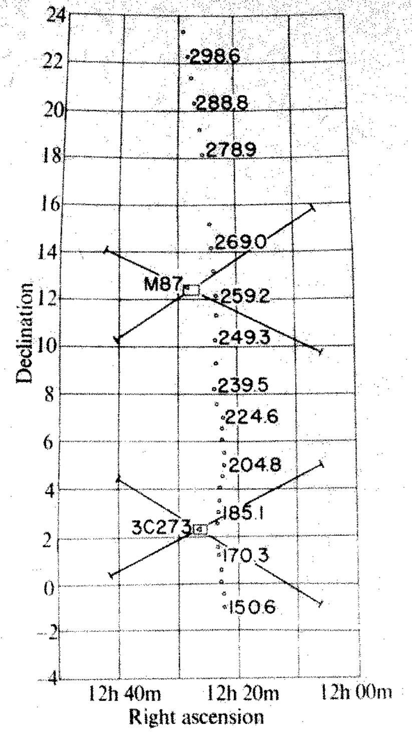

Fig. 1 Scan track across 3C 273 and M87. Each counter was equipped with a 1° × 8° collimator. The collimators were crossed as shown by the bars representing the 8° dimension. Open circles identify positions of the centre of the field of view at the indicated times in seconds from launch. Triangles give the positions of 3C 273 and M87 within error boxes of the measurements.

lished 2σ upper limits which are less than the flux claimed by the Rice University group, but a Rice University balloon observation in 1968 (ref. 9) produced essentially the same result as in the 1967 flight. It remains uncertain, therefore, on the basis of all of these balloon observations whether the spectrum does in fact extend to $E > 25$ keV without an increase in spectral index or whether the flux is variable.

The Virgo Cluster

M87 lies in the midst of the Virgo cluster which contains some 2,500 galaxies within a field of about 12 degrees diameter. About 80 per cent of the cluster was scanned by the detectors in our March 1969 flight, during the time interval 230 s to 280 s. The lower graph of Fig. 2 shows how the number of galaxies in the field of view varied with time. The signal from M87 stands above a general increase in background which may be associated with the large number of normal galaxies in the cluster. If we average the background from 230 s to 280 s, excluding the interval that contains M87, we obtain 17.3 counts per second which is about 7σ above the average of 13.7 counts per second for the background in the 280 s to 320 s interval outside the cluster. The increment of background flux amounts to 8×10^{39} erg s^{-1} per galaxy (1–10 keV) if the average distance is taken to be that of M87, 14.8 megaparsec, and the average spectrum is assumed to be a power law of index—1. In an analysis of the distribution of X-ray sources within our galaxy, we had estimated[10] a total X-ray luminosity for the galaxy of 7×10^{39} erg s^{-1} which is in close agreement with the figure we now obtain for the luminosity per galaxy from an average of 2,000 galaxies in Virgo.

Observation of 3C 273

In 1967 a scan was made of the position of the quasar 3C 273. There was some evidence[2] of X-ray flux at a level of about 2×10^{-10} erg cm^{-2} s^{-1} (1–10 keV) but the statistical measure of the signal did not exceed two standard deviations (2σ). If taken as an upper limit, the measurement implied that the X-ray power did not exceed 7×10^{45} erg s^{-1}. A simple extrapolation of the −0.7 radio-optical spectral index to the X-ray range would predict a flux of about five times the upper limit of the 1967 observation.

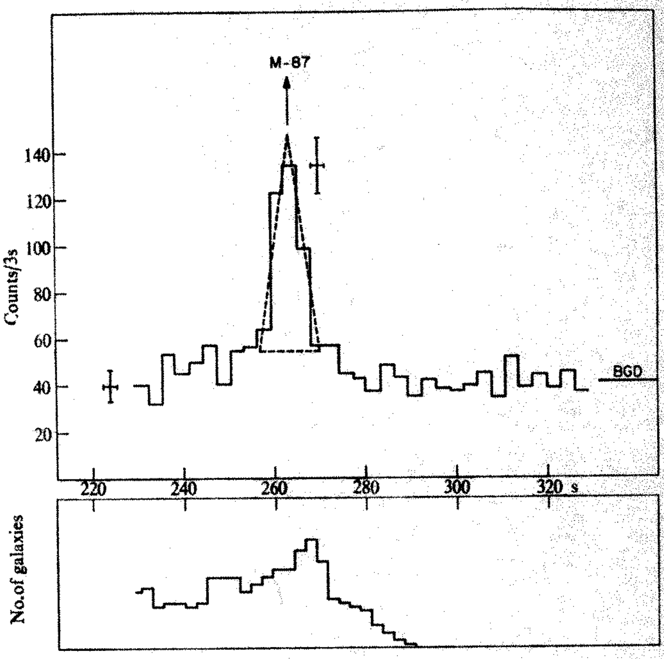

Fig. 2 Scan across M87. Signals from both counters were matched at their peaks and summed over the range shown above. The relative number of Virgo Cluster galaxies in the field of view of both counters is plotted below. BGD is the background level obtained by excluding the M87 signal and averaging the entire count from −2° to +22° declination.

A scan of 3C 273 was included in the March 1969 NRL flight with the results shown in Fig. 3. If background is taken to be the average over the entire 20 degree scan track from −2 degrees to +24 degrees declination (with the M87 counts removed), the peak signal at the position of 3C 273 stands 3σ above background. The spectral range was 1 to 4.5 keV and the flux was 6×10^{-11} erg cm^{-2} s^{-1}, about one-fifth of the flux from M87. The corresponding X-ray power is about 2×10^{45} erg s^{-1} for a distance of 500 megaparsecs.

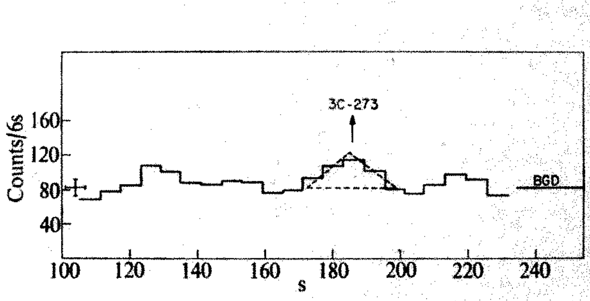

Fig. 3 Scan across 3C 273. Signals from both counters were matched at sec and summed over the range shown above. The controlled scan began at 150 s. Manoeuvres between 100 and 150 s included a large area of sky outside Virgo.

Bowyer *et al.* observed 3C 273 on June 14, 1969, and reported[11] a flux of 3×10^{-10} erg cm^{-2} s^{-1} (1–10 keV), which is several times greater than the flux which we observed less than three months earlier. It may be premature, however, to conclude that such high variability is characteristic of 3C 273, considering the marginal nature of the detections.

Discussion

In the radio spectrum, M87 is characterized as a core halo source (Virgo A). An extended optical jet emerges from the nucleus to a distance of at least 1,500 parsecs. The light of the jet is strongly polarized and the radiation mechanism is undoubtedly synchrotron. Recent refinements in both optical[12] and radio resolution[13] have revealed that the jet is composed of several optically bright knots, no more than a second of arc in diameter, and that the radio core contains a compact source with a diameter of 2.5 light months and a luminosity of 10^{39} erg s^{-1} in a band of 10^{10} cycles about a frequency of 0.23×10^{-10} Hz.

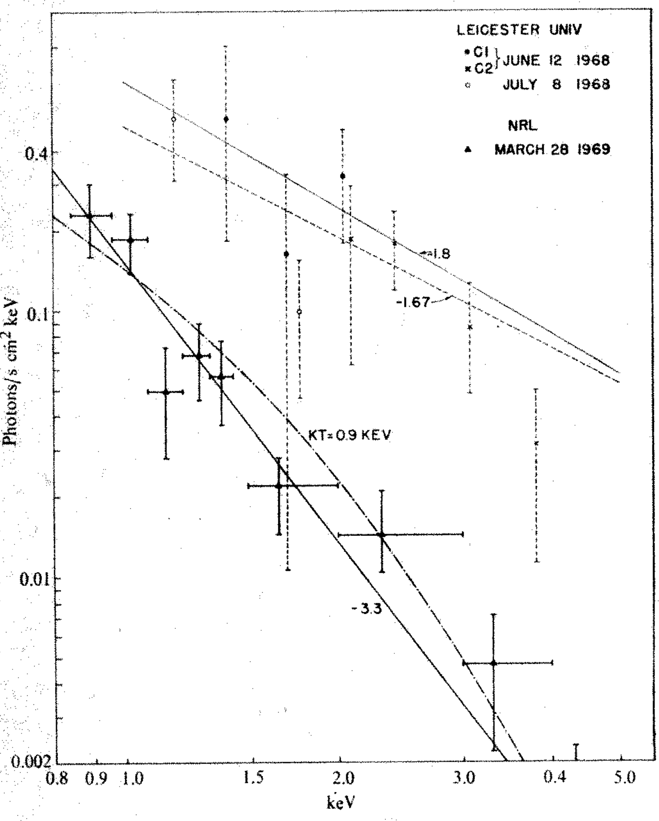

Fig. 4 Spectra of M87 obtained from two flights by the Leicester University group and the NRL flight described here. The photon power law indices are indicated on each curve. Also shown is a possible bremsstrahlung fit to the NRL data with $kT = 0.9$ keV.

When the earliest X-ray results at 1 to 10 keV were fitted to a single power law spectrum with index −0.7 extending all the way from radio through optical to X-ray wavelengths, this remarkable fit over more than nine decades of frequency suggested the possibility that synchrotron radiation generated by relativistic electrons emerging from the core and traversing the jet was responsible for the entire spectrum[14]. The lifetime of the electrons would, however, be too short to cover the distance from the core to the end of the jet even for the optical radiation—for an equipartition field of about 3×10^{-4} gauss, the optical lifetime is about 100 years. To avoid the problems of electron lifetime it was proposed[15] that relativistic protons are initially injected and interact with the ambient gas of the condensations in the jet to produce pions. The pions subsequently follow the π–μ–e decay sequence to yield relativistic electrons. Felten[16] has argued that this model suffers from difficulties in explaining the absence of gamma ray emission from π_0 decays. The predicted gamma photon flux of 4×10^{-10} cm^{-2} s^{-1} is well above the observational upper limit of about 5×10^{-11} cm^{-2} s^{-1}. He also pointed to the difficulty of accounting for enough ambient gas to balance the cosmic ray pressure in the condensations.

The evidence for variability in Table 1 and Fig. 4 lends support to models which associate the emission with the recently revealed compact sources in the nucleus and the jet. According to Burbidge[17], the energy density of radio photons and the energy content of relativistic electrons in the compact nuclear core may be sufficient to provide the observed X-ray emission by Compton scattering. Several years ago, Shklovsky[14] noted that the X-ray power of M87 is about three orders of magnitude greater than the luminosity in optical line emission from the core of the galaxy. If the X-ray source were concentrated in the nucleus, it would be enveloped by cold plasma which it would ionize and excite to line emission. The relative weakness of the line emission must therefore imply that only a very small part of the X-ray emission, if it originates in the core, is absorbed. Shklovsky therefore suggested the possibility that the core plasma was concentrated in several condensed bodies distributed with sufficient inhomogeneity so that only about one per cent of the core volume (radius 30 parsec) is obscured by these dense bodies.

Burbidge has also proposed that the knots on the jet may be clusters of massive compact objects, surrounded by magnetospheres, which are expelled from the nucleus. If these are pulsar-like stars, as many as 10^6 to 10^7 per optical knot would be required. Shklovsky[18] refers to large rotating magnetized plasma bodies as "magnetoids" and suggests that each condensation in the jet of M87 is a small magnetoid (10^4 $M_{\odot}$) similar to a quasar. The light radiated by the magnetoid should be variable in flux and polarization.

More accurate and complete information on this variability would provide important clues to the sizes of the radiating regions. Such data may be forthcoming from the recently launched X-ray astronomy satellite SAS-1 of NASA. The size of the jet in M87 is large enough (20 arc s) so that it is even within the realm of present day rocket astronomy to discriminate between emission from objects in the jet or from the nucleus.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Probability of Long Period Gravitational Radiation

BECAUSE there has been no published support yet for Weber's detection of gravitational waves[1], I venture to report an experiment at its early stages.

While several researchers have considered searching for gravitational radiation or supposedly related events[2] at relatively high frequencies, I considered looking in the low frequency range near and below 1 Hz. This is made possible through the method used in deep space probe tracking[3], which in recent years has obtained an accuracy of 1 part in 10^{12}. Basically, my experiment consisted of searching for variations in the expected Doppler frequency of signals returning to Earth from Mariner 6 or 7, while the spacecraft were at distances from the Earth comparable with the wavelength of such long period gravitational radiation that might exist.

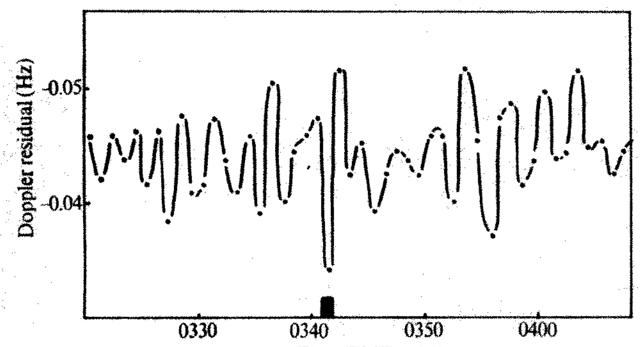

Fig. 1 Actual Doppler residuals remaining after taking out the correction for the spacecraft's calculated trajectory. The interval of significance (0341) is indicated by a black bar. These data are for Mariner 6 on March 15, 1969.

Unlike Kaufmann[4], my proposal was not concerned with the detection of the gravitational Doppler effects on the electromagnetic radiation. These are several orders of magnitude below the sensitivity of the present equipment. Rather I was concerned with detection of the direct effects of gravitational radiation on the spacecraft's trajectory.

For this experiment I was limited to sampling rate intervals of 60 s. I considered the difference in the dispersion factor between the frequencies of Weber (10^3 Hz) and those available to me for analysis (10^{-2} Hz) to be small, and so I considered near simultaneous events.

There were four records of Doppler data available, covering times of particular events indicated by Weber in his first report[5]. Because of a high background noise level, two of these were unusable. Of the others, the first indicated that something had occurred at the upper frequency limit of the data (0.0083 Hz). This event is seen in Figs. 1 and 2. Noise factors include variation of electron density along the path of propagation, ionospheric changes, instrumental stability, and long period gravitational radiation. Clearly something unusual happened around the interval of Weber's event at 0341 GMT on March 15, 1969.

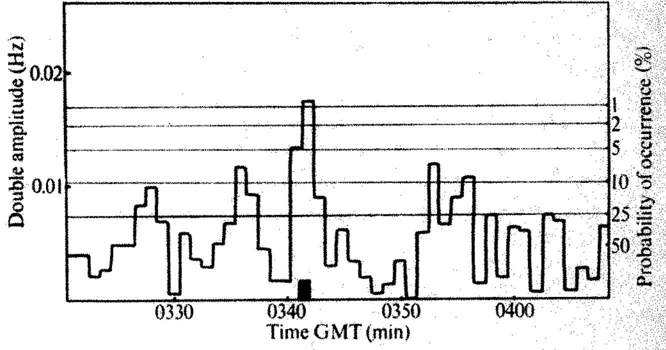

Fig. 2 The double amplitude 2 min period noise (0.0083 Hz). The probability of occurrence for such amplitudes for this day is given in per cent. The probability for the amplitude at 0341 is 0.7%.

Such gravitational waves as the one I have indicated cause a maximum velocity change of the spacecraft of less than 3 mm s^{-1} as seen from Earth. This, if integrated over an interval of 60 s, indicates a displacement of the body by ~10 cm over a total distance of measure between the Earth and spacecraft of approximately 10^{12} cm, a displacement of 1 part in 10^{11}. Weber measured 1 part displacement in 10^{15} at a higher frequency, using only a fraction of the wavelength. During a time interval 10^5 larger than Weber's I observed a relative displacement 10^4 larger. The form of the Doppler pattern indicates that the disturbance caused a dilatation at onset across the detector system. This is what was expected from a gravitational wave, unlike some other noise sources. On the other record, 0312 GMT, March 21, 1969, I observed longer period disturbances (10^{-3} Hz) indicating similar velocity changes and a similar Doppler pattern. Generally one should expect greater velocity changes between 10^{-2} Hz and 1 Hz. This region will be investigated later, when I can obtain sampling rate intervals of 1 s, not available for normal tracking purposes. Smaller sampling rate intervals contain more noise, but it is not expected that the amplitude

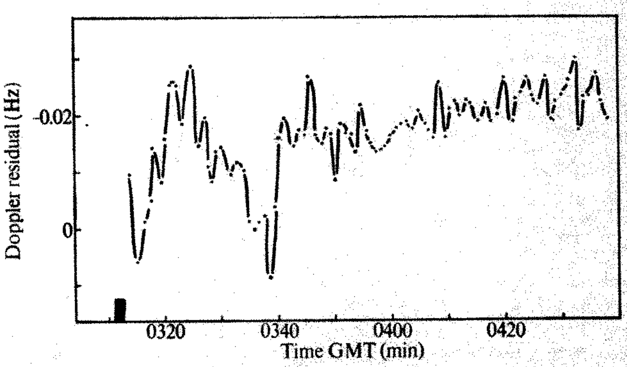

Fig. 3 Actual Doppler residuals following the event of 0312 GMT, March 21, 1969. This is plotted 1/2 scale to the previous event. Such large disturbances rarely occur.

of this noise will generally increase as rapidly as the amplitude of the gravitation radiation; more coherent patterns can be established.

According to Weber's most recent results[6] the most probable direction of these waves is aligned with the direction of the galaxy centre. Using this method the response is therefore directly a function of cos α, where α is the angle between the line of sight to the spacecraft and the direction of the galaxy centre. It is hoped that with refinements in analysis, shorter sampling rates, and wavelength and angle determinations, future correlations can be improved considerably. Indeed, with the present sampling rate, I did not expect a favourable result.

I thank Jack Lorell of the Tracking and Orbit Determination Section of the Jet Propulsion Laboratory in Pasadena for Doppler tracking data, and Joe Weber, who inspired these observations.

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Abundances and Acceleration Mechanisms of Cosmic Rays

MEASUREMENTS of the chemical composition of cosmic rays[1] have shown that for most elements the abundances roughly correspond to their universal abundances. I wish to point out here that some systematic differences occur in the low energy range, which are correlated with the first ionization potentials of the corresponding elements.

In Fig. 1 I have plotted the ratio of the cosmic ray abundance[1] to the "normal" stellar abundance[2] for the different elements. The results are given for cosmic ray abundances in three different intervals. The elements Li, Be, B and F are omitted from the figure. The large overabundances of Li, Be and B are probably due to spallation. The element F is undetected in several energy ranges, but may be overabundant in the 50–200 meV/nucleon range. The uncertainties in the cosmic ray abundance and "normal" star abundance are, however, large.

It is apparent from Fig. 1 that there is a significant correlation between first ionization potential and relative abundances of the cosmic rays in the lowest energy range. The relative abundances range from an overabundance of the order of 10 for elements with the lowest first ionization potentials to underabundances of the order of 10 for elements with the highest first ionization potentials. In the energy range 200–5,000 MeV/nucleon the same correlation may also be present while the picture seems to be more complicated for the highest energy range. In this energy range the correlation is possibly present for the lighter elements up to Ca. On the other hand, for the elements from Sc through the iron group and up to Ni there is no systematic behaviour in terms of the first ionization potential. These elements have approximately equal first ionization potentials but their relative cosmic ray abundances range from an overabundance of more than 1,000 in the case of Sc to a nearly normal abundance for Fe.

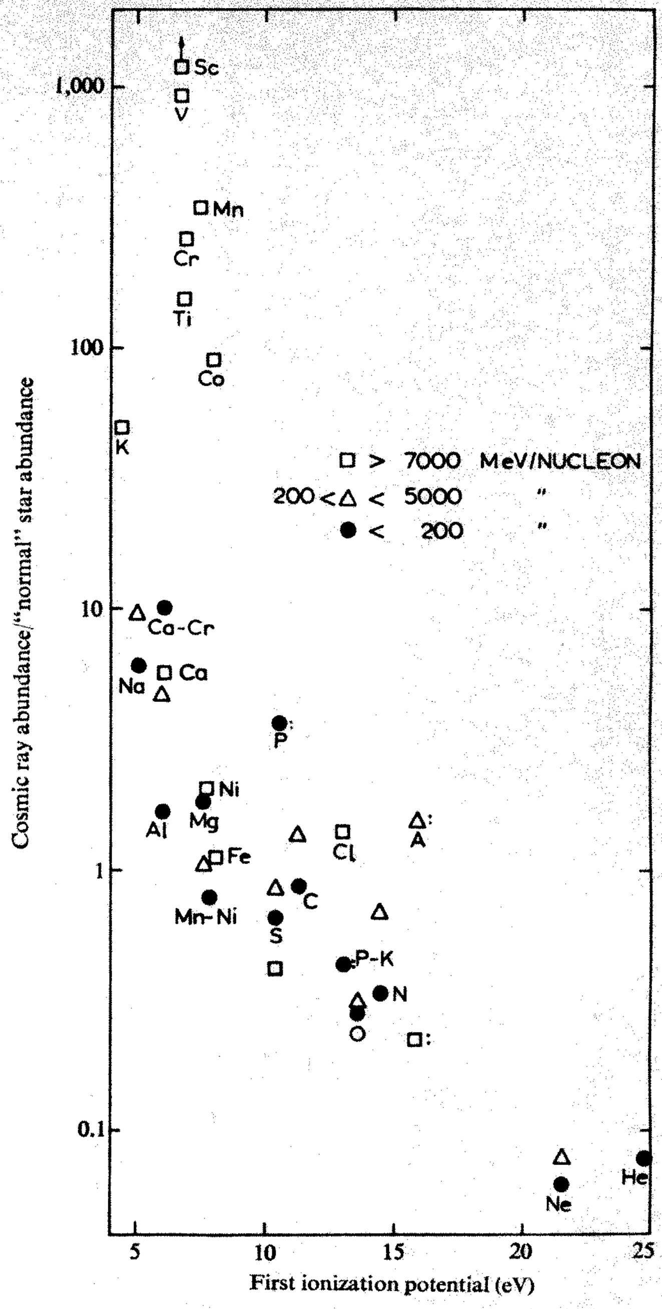

Fig. 1 The ratio of the cosmic ray abundance for the different elements at three energy intervals to the "normal" star abundance against the first ionization potential of the corresponding elements. For the "normal" star abundance, I used an average of the results given by Unsöld[2] with the exception of the abundance for A which was taken from the work of Pottasch[4] and the solar abundance for Fe which was taken from the work of Garz *et al.*[5].

The observed correlation at the lower energies suggests strongly that low energy cosmic rays have initially been accelerated in a process where electromagnetic forces have acted on a gas of normal composition that is partly ionized as a consequence of normal thermal or radiative processes. In such a gas the elements with low first ionization potentials are preferentially ionized and may therefore be accelerated by the electromagnetic forces. But the elements with high first ionization potentials are less likely to be ionized and will therefore have a smaller probability of being accelerated. I do not expect a violent event, in which the overall ionization state is high, to give rise to the observed cosmic ray abundance spectrum at low energies. Such violent events may be a more likely explanation for the cosmic rays at higher energies.

The findings reported here apparently require more than one type of cosmic ray source. This is in accordance with the conclusions reached by Comstock[3] on the basis of the shape of the energy spectrum at low energies.

Possible regions of partly ionized matter accelerated by electromagnetic forces are (i) shells of supernovae, in which the accelerating force may be the magnetic field of a rotating magnetized neutron star, and (ii) the HII regions around rotating magnetic Ap stars. I have considered this process elsewhere (unpublished work) and found that the energy input in this case may be somewhat in excess of 10^{-27} erg cm^{-3} s^{-1}.

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Large Decrease in the Clear Air Transmission of the Atmosphere 1.7 km above Los Angeles

ASTRONOMICAL measures of atmospheric extinction, routinely carried out during most programmes of astronomical photoelectric photometry, provide a large sample of data of importance to studies of long term anthropogenic pollution of the atmosphere[1]. We have therefore begun an exhaustive compilation of present and past measures of extinction at as many observatories throughout the world as possible. I wish to point out one of the most important results so far, the measurement of a large secular decrease in the transmission of the atmosphere measured at a significant altitude above the Los Angeles Basin.

In 1911, Abbott[2] published the results of his measures of the transmission at various wavelengths of the atmosphere above Mount Wilson, California, which is on the rim of the Los Angeles Basin, 1,742 m above and 11 km horizontally from the centre of Pasadena, and 25 km from downtown Los Angeles. Fig. 1 shows a plot of his data for four wavelengths, in the ultraviolet, blue, yellow and red, given in units of atmospheric extinction by magnitudes, as conventionally determined by astronomers[3].

In the years just before the advent of frequent occurrences of smog at these altitudes, which became important beginning in about 1962, I measured the atmospheric extinction in three wavelengths on 31 clear, smogless nights at the Mount Wilson Observatory. Measures were made in the standard way with photoelectric photometers attached to the 60 inch and 100 inch telescopes. The mean extinction coefficients are also plotted in Fig. 1, where they are compared with Abbott's values found just over 50 yr previously.

The differences in the extinction coefficients are striking: 0.27 mag. in the ultraviolet, 0.09 mag. in the blue and 0.10 mag. in the yellow. These are large differences, especially considering that the data for the 1960s were taken only on nights when no trace of smog was detectable by tests for transmission variability. The fact that the early data are for daytime and the latter data are for night-time cannot conceivably account for this difference.

Table 1 Decreases in Atmospheric Transmission at Mount Wilson

Wavelength (μm)	50 yr decrease (%)
0.35	26
0.44	9
0.55	8

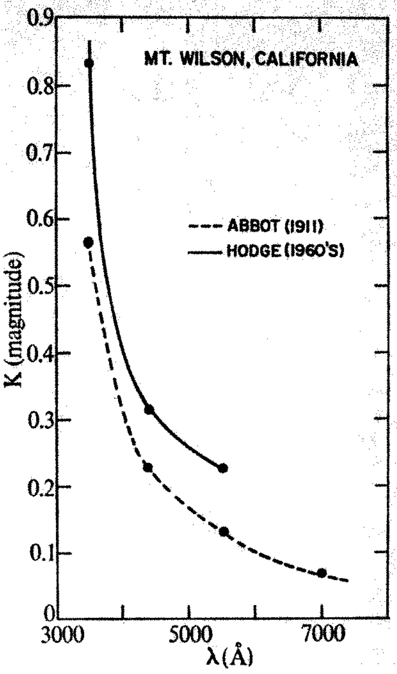

Fig. 1 A comparison of clear air extinction coefficients (in astronomical magnitudes) for the Mount Wilson Observatory for a period before 1911 and for nights in the years 1960–1962.

Table 1 gives the percentage decrease in the transparency that is indicated by these figures. It shows that the apparent secular change in the clear air transparency for this site, far above the Los Angeles Basin, is as large as 26% in the ultraviolet during this crucial period. This is clearly an important example of how astronomical current and archival data of this sort can be useful in studies of atmospheric aerosol pollution, which have taken on a recent urgency because of speculation on the possible effects on world climate[4–6].

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Shear Wave Propagation in Rocks

WE have demonstrated striking similarities in elastic wave propagation through rocks and single crystals in recent experiments. In particular, we find that two shear waves with displacements perpendicular to one another and with differing velocities are often propagated through rocks. This is illustrated in Fig. 1 at 5 kb pressure for samples of slate and dunite; an ultrasonic technique described by Birch[1] was used. One MHz AC-cut quartz transducer generated and received the shear waves, and an electrical pulse of 50 V was used to excite

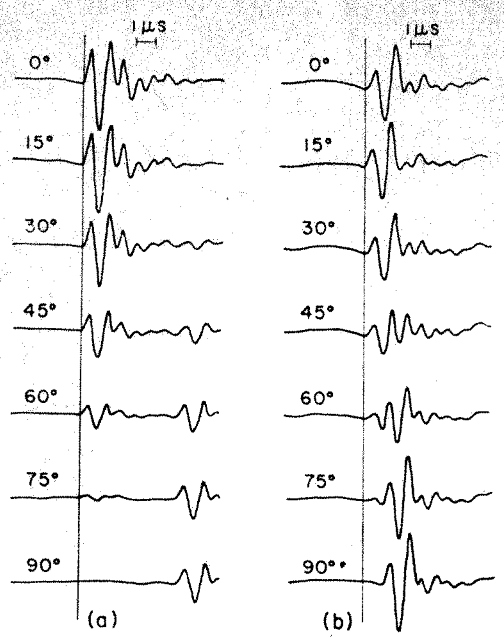

Fig. 1 Oscilloscope traces for shear wave propagation through (*a*) slate from Poultney, Vermont, and (*b*) dunite from Twin Sisters Peaks, Washington. The transducers are oriented at 0° to receive the higher velocity shear wave. Rotation of the transducers through 90° emphasizes the first arrival of the slower of the two shear waves.

the transducers. The rock samples were cylinders 2.54 cm in diameter and approximately 6 cm long.

For the slate the propagation direction of the shear wave was parallel to the cleavage. The transducers were rotated in steps of 15° such that shear waves were first propagated with a displacement direction parallel to the cleavage. Fabric study of the dunite shows a strong concentration of olivine *a* crystallographic axes and girdles of *b* and *c* axes. Propagation in the sample shown in Fig. 1 was normal to the *a* axes concentration.

Two shear waves with differing velocities are obviously propagated through both rocks. Velocities for the two shear waves in the slate differ by approximately 1 km s^{-1}, whereas velocities of the two waves in the dunite differ by 0.3 km s^{-1}. The latter value seems to be quite typical for shear velocity anisotropy in dunites. The phenomenon is common in metamorphic rocks and has been observed in several igneous rocks. The time resolution did not always permit clear identification of the two shear waves, but a rotation of the transducers produced a change in shape of the first arrival which strongly suggests the presence of this type of anisotropy. In all cases the observed anisotropy seems chiefly to be the result of preferred mineral orientation.

The importance of this study for shear wave propagation within the Earth remains to be established. The recognition of two shear wave arrivals would, clearly, provide unequivocal evidence for seismic anisotropy in regions of the upper mantle where longitudinal waves appear to vary in velocity with azimuth. It is highly probable that many regions of the Earth's crust and mantle are anisotropic and, hence, two shear waves should be propagated through these regions. It is possible that the arrival of one of the shear waves is often masked by the arrival of other energy.

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Measurement of Tilt of a Frozen Sea

IN May 1967, as part of a programme of geodetic studies in the vicinity of the North Pole, an attempt was made to measure the tilt of the fluid surface of the Arctic Ocean. Three holes were drilled through the ice and the tilt relative to the equipotential surface was determined by levelling from hole to hole with a levelling instrument[1]. Two sets of observations were taken at a distance of about 56 km from the North Pole on May 11 and 13, 1967. Both measurements showed a downward tilt of 8 ± 2 seconds of arc in the direction of 100° and 150° west of Greenwich, respectively. This experiment showed that, if the measurements are correct, large ocean tilts in the polar region may occur. However, because of atmospheric refraction, this technique is not suited for the desired degree of precision and the search for a better method led to the development of a hydrostatic levelling system that was tested in the vicinity of the North Pole in April and May 1969 and in the Gulf of St Lawrence in March 1970[2].

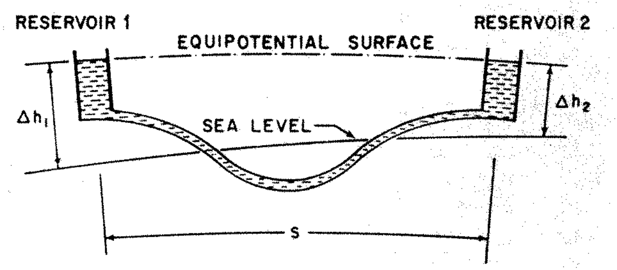

Fig. 1 Schematic diagram of hydrostatic levelling system. The tilt α is $\frac{\Delta h_1-\Delta h_2}{s}$. The instrument dimensions are: tube length 120 m, tube diameter 1.27 cm, reservoir height 12 cm and reservoir diameter 4.6 cm. The system is filled with a low viscosity silicone fluid.

Fig. 1 illustrates the system schematically. Two water wells are formed by drilling and freezing electrically heated, insulated pipes into the ice, 120 m apart. The hydrostatic level consists of two reservoirs bolted to the wells and connected by a horizontal tube. The usual problems associated with hydrostatic levelling systems required that the tube is positioned as nearly horizontal as the terrain allows. The system is filled with a low viscosity silicone fluid. If it is not moving, and under conditions of equal atmospheric pressure at the wells and constant fluid temperature throughout the system, the fluid surfaces in the two reservoirs form part of the same equipotential surface. If Δh_1 and Δh_2 are the level differences between the fluid levels of the reservoirs and the ocean surface and s is the separation between the two reservoirs, then the tilt is $\frac{\Delta h_1-\Delta h_2}{s}$. The level difference $\Delta h_1-\Delta h_2$ is determined by measuring the level differences f_1, w_1, f_2, w_2 relative to a level plate using pointed measuring rods connected to micrometers. The sensitivity of the system is given by the ratio of the smallest fluid level difference $\Delta h_1-\Delta h_2$ that can be measured, and the level length s. External effects, listed below, cause a displacement of the fluid levels, contributing to an apparent tilt if not monitored and corrected for. In developing the system we attempted to keep the measurement of the level difference $\Delta h_1-\Delta h_2$ within a standard deviation of $\pm2\times10^{-5}$ m, resulting, with a level length of $s=120$ m, in a sensitivity of $\pm1.6\times10^{-7}$ radians. The threshold values of external error sources above which corrections have to be applied (Table 1) are therefore reached when the resulting level displacements exceed $\pm1.0\times10^{-5}$ m.

(1) As long as the connecting tube is perfectly horizontal only the temperature differences of the fluid between the two reservoirs matter. It is measured to an accuracy of ±0.01° C using thermistors. (2) The possibility of density changes of the

seawater in the wells is avoided by pumping the old water out of the wells before each measurement. (3) Atmospheric pressure gradients in excess of 30 μbar km^{-1} are rare. (4) V_1 and V_2 are the current speeds of the water flowing past the bottom openings of the wells which cause a pressure decrease in the wells. The Bernoulli effect is insignificant for current speeds of less than 8 cm s^{-1}. During periods of rapid drift the flow rate must be measured with current meters. (5) The component of the acceleration in the direction of the level axis and (6) the velocity component at right angles to the level axis must be considered. The system is made insensitive to vertical accelerations (wave motions) by choosing its dimensions such that the dynamic response of the level fluid is critically damped.

The pack ice commonly drifts at speeds and accelerations which are a magnitude larger than the threshold values. Therefore of all external effects, the system is most sensitive to drift speed and accelerations. Precise navigation is therefore a prerequisite to precise tilt measurements.

Table 1

Error source	Threshold value
1. Temperature of the hydrostatic fluid	±0.06° C
2. Density change of the well water	$\pm 5 \times 10^{-6}$ g cm^{-3}
3. Atmospheric pressure gradient	30 μbar km^{-1}
4. Differential flow (Bernoulli effect)	$V_1^2 - V_2^2 < 2$ cm^2-s^{-2}
5. Horizontal accelerations	1.6×10^{-4} cm s^{-2}
6. Drift velocity (Coriolis force)	1.1 cm s^{-1}

Table 2

	Level I	Level II
Date	April 30/69	May 2/69
Position	89° 29.2′ N, 31° 30′ W	89° 25.0′N, 21° 00′ W
Time (GMT)	0200	2200
Drift speed (cm/sec, constant)	5.6	1.8
Direction of drift	300°	56°
Direction of level axis	248°	129°
Observed tilt *	4.71 ± 0.07	3.15 ± 0.08
True tilt (Coriolis corrected) *	5.22 ± 0.07	3.23 ± 0.08

* Down-slope in direction of level axis, in units of micro-radians.

The results of the tilt measurements near the North Pole determined with two hydrostatic levels are listed in Table 2. Directions are west of Greenwich. The observed tilt has been calculated from the mean of 40 measurements of the level differences f_1, f_2, w_1, w_2 (Fig. 1) after corrections for the temperature changes of the reservoir fluids had been applied.

Tilt observations in the Gulf of St Lawrence were carried out in an area between Amherst Island and the eastern tip of P.E.I. The sea surface sloped down in a northerly direction. Preliminary results show that the observed tilt ranges from −0.4 to 3.5 micro-radians[2].

We have shown an experimentally tested method which allows us to measure the tilt of a frozen ocean with high accuracy. We believe that it is important, from both geophysical and oceanographic points of view, to use automatically recording sensors of this type over baselines which are of the order of 10^2 km to determine the extent and persistence of ocean tilts. As part of a proposed international study of ice deformation, known as Arctic Ice Dynamics Joint Experiment, it is hoped to set up four pairs of sensors at the corners of a 100 km square with an additional pair in the centre. These would permit the statistical calculation of planar, quadratic and cubic tilt surfaces with varying degrees of overdetermination, since there will be ten distinct measurements of ocean tilt at these five stations.

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Baffin Bay—an Ocean

RECENT theories of the opening of the Atlantic Ocean and the Labrador Sea and of the relationship of the assumed motions to the history of Baffin Bay lead to contradictory opinions about the nature of the crust beneath the bay. The fit of the continents[1] and the similarities of the rock types and their ages along the opposing coastlines of Greenland and Northern Canada[2,3] suggest that the two have separated by continental drift. Geophysical studies in the Labrador Sea (unpublished work of X. Le Pichon, R. D. Hyndman and G. Pautot) imply that Baffin Bay was formed by seafloor spreading and therefore that oceanic crust should lie beneath it. Conversely, from an interpretation of the geology along the coastlines, the present configuration of the bay has been attributed to the extension of continental material and subsequent faulting among its margins[4]. The latter hypothesis is supported by a study of

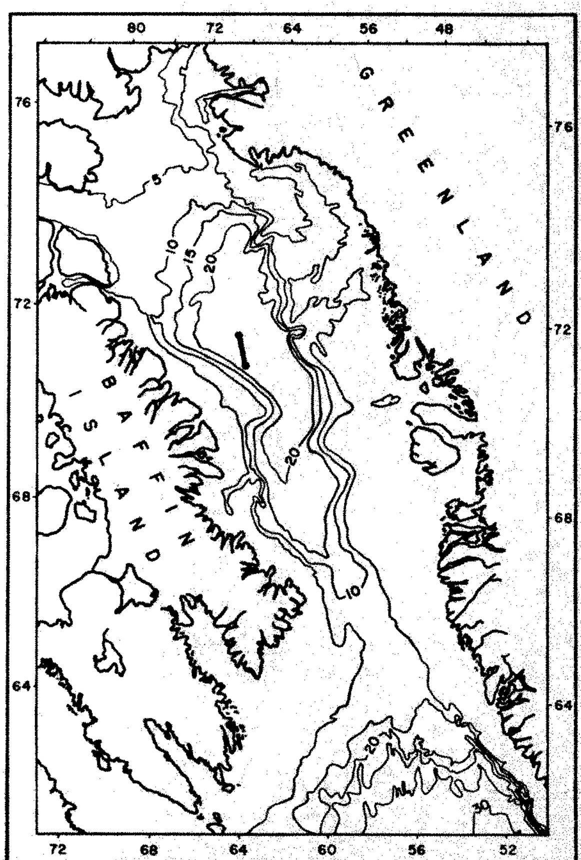

Fig. 1 Location of the refraction line (the heavy black line). The bathymetry contours are in hundreds of metres.

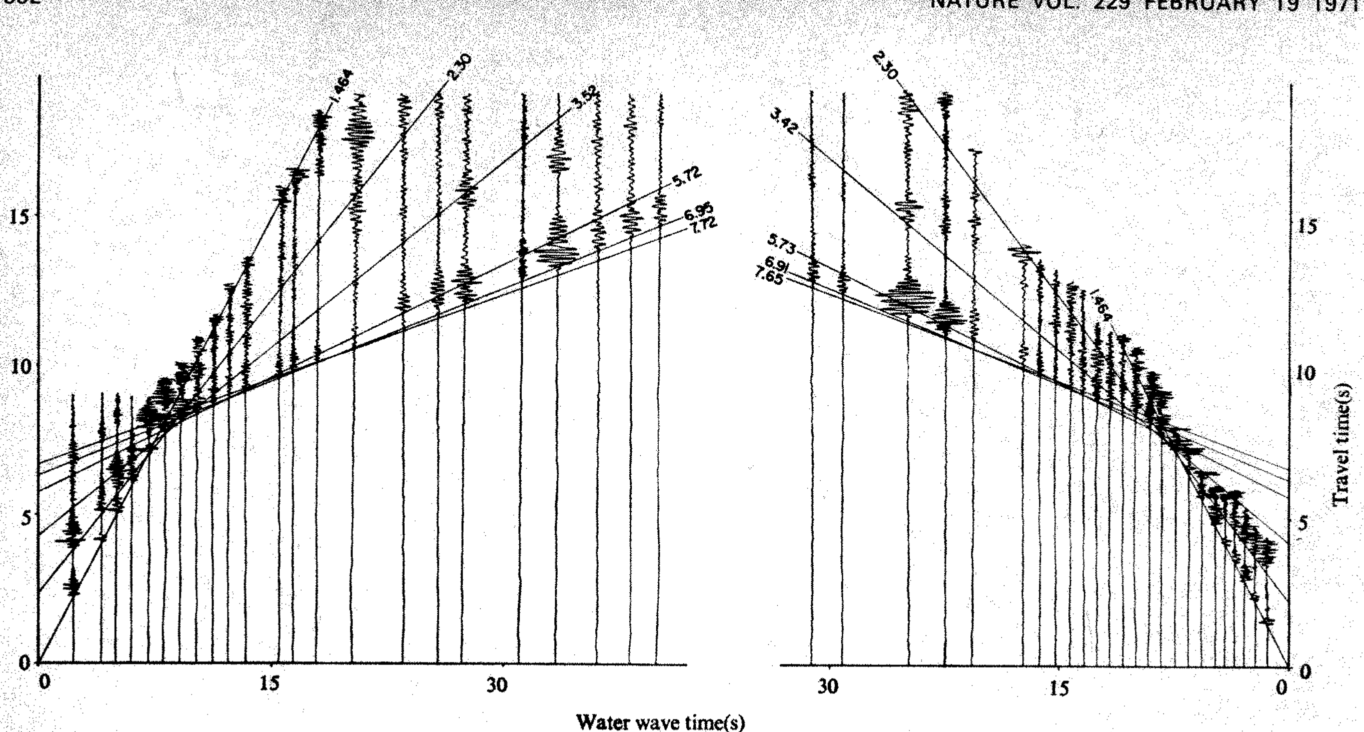

Fig. 2 The record stations. Velocities are in km/s. The right-hand figure shows recordings at the southern station and the left-hand figure shows recordings at the northern station.

surface waves[5] which showed that the Lg phase is transmitted across the area. This surface wave is generally associated only with continental crustal structure. The lack of any positive evidence which could be used to resolve this controversy prompted us to conduct the experiment described here.

A two-ship seismic refraction line was performed in the deep region of Baffin Bay in October 1970 (Fig. 1). CSS Hudson acted as the recording ship and USCGC Edisto as the shooting ship. The line was reversed ; however, the second shot line did not coincide exactly with the first due to ice conditions at the two ends of the proposed line. The two resulting shot lines did not diverge by more than 18 km. Also, Hudson drifted about 12 km and 6 km respectively at the southern and northern receiving stations during the listening periods. The positions of the shot lines were determined by LORAN navigation and the location of the receiving stations by satellite fixes. The explosive charges were fused fired and the charge sizes ranged from 30 to 500 pounds (13 to 230 kg).

Corrections were applied to remove variations in the travel times due to bottom topography along the shot lines and beneath the receiving stations. The constant water depth to which all travel times have been corrected is 2.30 km. Shot to receiver ranges were obtained from the direct water wave arrivals using a velocity of 1.464 km/s for sound in seawater. This value was calculated from previous measurements of temperature and salinity in central Baffin Bay[6]. Recordings of all shots were appropriately arranged and are presented as record sections in Fig. 2.

Five crustal velocities are shown on each record section. The velocities of 7.7 km/s and 6.9 km/s are well established, the former by first arrivals and the latter by good second arrivals. The 5.7 km/s velocity is defined by first arrivals over a small distance interval—this is best seen on recordings at the northern station. The values of the two lower velocities, 2.3 and 3.5 km/s, have been assumed; however, their values are not critical to the results reported here.

True velocities and the layer thicknesses were calculated and these are shown in Table 1. The velocities, 5.7, 6.9 and 7.7 km/s, are similar to those measured for layers 2 and 3 and the M discontinuity respectively in the ocean basins[7], and we shall use this terminology in the following discussion. The total depth to the M discontinuity from the sea surface is 11 km including 4 km of sediment. This depth and the layer velocities bear no similarity to continental crustal values but are closely related to those obtained in oceanic areas. There are, however, several differences. The unusually thick sedimentary cover is substantiated by reflexion profiling results, and in view of the landlocked nature of Baffin Bay a thick sequence of sediments is not unreasonable. The thickness of layer 2 is similar to that measured in the deep ocean basins but the thickness of layer 3 is appreciably less. If the deep central portion of Baffin Bay was formed by seafloor spreading, the lesser thickness of basaltic crustal rocks could be attributed to a different rate of outpouring of crustal material or to a different spreading rate than is at present observed at active ridges.

Table 1 Layer Thicknesses and Velocities

Layer	Velocity (km/s)	Thickness (km) Southern station	Northern station
Water	1.464	2.3	2.3
Unconsolidated sediment	2.30	2.1	2.0
Sediment	3.47	2.0	2.3
Layer 2	5.72	2.0	2.1
Layer 3	6.93	1.9	2.1
Mantle	7.68	—	—

The positions of the southern and northern stations were 71° 39′ N, 65° 55′ W and 72° 18′ N, 66° 13′ W respectively. These are median positions taken during the time that Hudson was on station.

The velocity of the mantle rocks, 7.7 km/s, is slightly lower than that normally found in the ocean basins. It is not, however, significantly less than the mean measured beneath the Eastern North Atlantic basin[7], for example, 7.85 km/s with a standard deviation of 0.18 km/s. Also, the mantle velocity may be lower because the M discontinuity is shallower and the pressure less at the base of the crust here than in most other oceanic regions. Therefore, it would be unrealistic, though perhaps tempting, to attribute the low mantle velocity to "anomalous mantle" material often associated by some workers with mid-ocean ridges[8].

In conclusion, both the thickness of the crust and the measured velocities show that the central deep portion of Baffin Bay is oceanic and that it cannot be attributed to extended and faulted continental material.

We thank the masters, officers, crew and the scientific parties of CSS Hudson and USCGC Edisto for their help. This work was part of the Hudson-70 expedition organized by the Atlantic Oceanographic Laboratory of Bedford Institute as a Canadian contribution to the International Decade of Ocean Exploration.

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Supernovae and the Extinction of the Dinosaurs

WE wish to suggest that a nearby supernova explosion might produce climatic effects so drastic as to cause the extinction of many animals, including the dinosaurs. Earlier discussions of this topic[1,2] focused on the radiation doses to be expected as a result of the interaction of high-energy cosmic rays and γ-rays with the atmosphere. Reasonable estimates of the parameters involved implied doses which may account for some of the patterns of mass extinction observed in the geological record.

The belief that large fluxes of cosmic rays and γ-rays are produced during the early phases of a supernova outburst has been strengthened by the discovery of pulsars. In addition we might expect supernovae to be powerful emitters of soft X-rays during the first few days, as suggested by the identification of several features in the spectrum of type I supernovae as forbidden lines from highly stripped ions such as exist in the solar corona[3]. This requires that the expanding envelope have a temperature of the order of a million degrees, and suggests the existence of large X-ray fluxes. In general, if the efficiency of production of visible light relative to the production of high frequency radiation is small, of the order of a few per cent or less, then $\sim 10^{50}$ ergs in X-rays will be emitted in about a week as a result of a supernova outburst. It will soon be possible to verify or disprove the existence of large X-ray fluxes from supernova outbursts by satellite observations of supernovae in other galaxies[4].

Estimates of the probabilities for nearby supernovae show that ~ 1 supernova explosion should occur within a distance of 100 light years every 50 million years[1]. As a result of such an explosion, the atmosphere as a whole would absorb about 10^{28} ergs in X-rays in about a week or less, mostly in the ozone layer and the ionosphere between about 20 and 100 km, depending on the spectrum of the radiation. This is a hundred times the far ultraviolet and X-ray flux received from the Sun during a week[5].

The climatic effects of an enormous deposition of energy into the upper atmosphere are difficult to assess. London[6] has suggested that heating at the top of an atmosphere produces ascending motions in the stratosphere which make the lower atmosphere unstable or aid in the vertical exchange of momentum. Sudden increases in the short wavelength ultraviolet and X-ray emission from the Sun have been followed after a few days by a shift of the atmospheric circulation toward a pattern with definite glacial characteristics[7]. In our case the effect must be catastrophic, for the energy deposited in the upper atmosphere is of the same order as the gravitational binding energy of that part of the atmosphere above 60 km. It is also of the same order as the total kinetic energy of the atmosphere[8]. Thus, we can expect that the entire atmospheric circulation system will be profoundly modified. This will undoubtedly have disastrous short term effects with many storms of extreme intensity generated.

Willett[9] has speculated that climatic changes in general, and the ice ages in particular, are the result of significant variations of the ultraviolet emission of the Sun. The variation under discussion here is of a short duration, but because of its extraordinary intensity it may have long term ($\sim$years) effects through a change of the albedo resulting from the formation of very high altitude ice clouds, or the alteration of the greenhouse effect due to the disruption of the ozone layer and the general large scale mixing of the atmosphere. Long term effects seem to be predominantly of a kind that produce increased storminess and lowering of temperatures over much of the Earth.

These effects are not necessarily unique to a supernova explosion. An intense source of high energy radiation is all that is required. Another possibility is an anomalously large solar outburst.

Although disputed by some[11,12], the latest Cretaceous and earliest Tertiary (Maestrichtian and Danian stages) have generally been recognized as a brief interval during which many organisms underwent a severe attenuation in diversity or became extinct[13,14]. Among these were phytoplankton[15], planktonic foraminiferids[16], many forms of bivalve and cephalopod molluscs[17], echinoids[17], mosasaurs, plesiosaurs, marine turtles and dinosaurs[18].

Typically Mesozoic marine faunas are found above erosional paraconformities ("hard grounds") in Maestrichtian carbonate deposits in Europe[19] and the latest Cretaceous "Lancian" dinosaur fauna persisted through the time of maximum development of the Hell Creek floodplain in the western interior of North America, so that restrictions of epicontinental seas did not cause a serious attenuation of Mesozoic biota. Impoverished Danian faunas are, however, often separated by a bedding plane from Cretaceous faunas of similar sedimentary facies, and Newell's[20] implication that the intervening extinctions may have lasted considerably less than a million years seems to be reasonable.

It has been suggested that dinosaurs were gradually declining in taxonomic diversity during the latter part of the Cretaceous. This cannot be demonstrated because of the much smaller sample of Lancian dinosaurs relative to available specimens of Campanian forms[26], a lack of careful systematic studies of the groups, and limited area of the Earth from which the extrapolation is essentially founded (western interior of North America). Even if a decline should be documented in this region, a gradual climatic deterioration correlated with the southward shift of climatic zones, rise of Laramide ranges to the west and withdrawal of the interior sea may account for faunistic changes and yet not be linked to the causes of the extinctions at the close of the Cretaceous. Although ichthyosaurs probably declined to extinction before the end of the Cretaceous (ref. 27 and field records of the American

Museum of Natural History), and ammonities suffered a marked decline during the latter part of the period[17], neither phenomenon seems to be directly linked to the extinctions at the Cretaceous–Tertiary boundary.

The globally depauperate Danian biota[13], characterized by forms of a boreal aspect even in low latitudes[21], suggest that a temperature drop was involved in the extinctions at the end of the Cretaceous. Lowenstam and Epstein's[22] observation that water temperatures in Denmark during the lower Maestrichtian and upper Danian were similar implies that any such cool interval would have been short. Nagappa's[23] suggestion that ". . . a sudden though short lived cold period, not necessarily intense enough to bring about an ice age, was the cause of (the extinctions terminating the Cretaceous)", is not precluded by existing palaeobiological evidence.

In summary, the biostratigraphic record does not provide compelling support for considering global regressions of epicontinental seas or long term climatic trends as causative of the extinctions at the close of the Maestrichtian. It does suggest that the extinctions were of unusual magnitude and geologically brief duration, and may have been accompanied by a thermal drop. Eroded surfaces capping marine Maestrichtian sediments in stable tectonic areas may have been produced contemporaneously with the extinctions.

The biota of the Earth, which had not experienced widespread rigorous conditions for perhaps a hundred million years, probably would not have adjusted to the sudden onset of cool conditions as well as the modern biota. The disturbance of thermal stratification in the oceans by initial atmospheric turbulence, followed by several years of depressed temperatures, would dampen primary production in the oceans, concomitantly exterminating many forms in higher tropic levels[24]. Atmospheric turbulence in conjunction with normal tidal currents may have results in the erosion of bottom sediments in many areas[25], thereby accounting for the widespread occurrence of a paraconformity separating Maestrichtian and Danian sediments in otherwise complete stratigraphic sections.

The supernova theory does not conflict with the record of extinctions at the Cretaceous–Tertiary boundary as at present understood. It has merit in that its predicted effects can be compared to the record to a greater extent than some other theories of mass extinction.

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BIOLOGICAL SCIENCES

Isolation of the Cholinergic Receptor Protein of *Torpedo* Electric Tissue

LEE and his co-workers have reported[1-3], and we have confirmed, that α-bungarotoxin (α-BuTX), a component of the venom of a Formosan snake (*Bungarus multicinctus*), blocks specifically and irreversibly the depolarizing action of acetylcholine at vertebrate neuromuscular junctions. We wish to report that this toxin similarly blocks the cholinergically innervated electric tissue of *Torpedo marmorata*, and to describe isolation of the single membrane protein to which the toxin is bound.

The electric tissue of *Torpedo* was chosen as a source of cholinergic receptors because of its special structure[4,5] and its extraordinarily rich cholinergic innervation[6,7]. Each electric organ is composed of about 500 columns of electroplaques, and each column has hundreds of cells. Judging

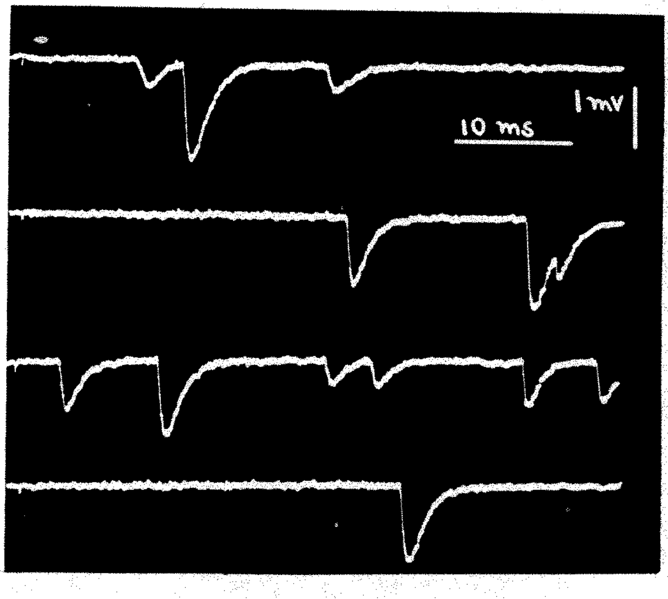

Fig. 1 Miniature synaptic potentials recorded extracellularly from an isolated piece of electric tissue. The potentials are a consequence of multimolecular amounts of acetylcholine acting on the membrane of an electroplaque, at about 23° C.

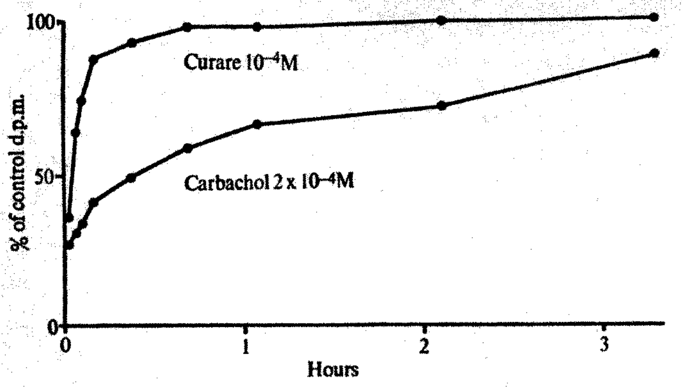

Fig. 2 Effect of d-tubocurarine and carbamylcholine on the binding of α-bungarotoxin to isolated membranes. Membranes from approximately 200 mg of electric tissue were incubated at 20° C in 1 ml. of buffer with or without the drugs indicated for 1 h, and then with 0.5 µg/ml. of ^{131}I-α-bungarotoxin in addition for the times shown. The membranes were washed twice by sedimentation at 20,000*g* for 1 min and resuspension in fresh buffer, before being dissolved in an alkaline solvent for liquid scintillation spectrometry.

from freeze-etchings in which the fracture plane was that of the synaptic cleft (Nickel and Potter, unpublished; compare ref. 5), these thin flat cells are innervated over a large part of their ventral surfaces; and because of grooves and infoldings in the postsynaptic membrane, it seems reasonable to consider that the area of postsynaptic membrane is comparable with the total "flat" ventral cell surface. In the fresh organs of one small fish we have estimated that there were an average of 13,000 plaques per gram of tissue having a combined "flat" ventral cell surface area of 0.07 m^2. The tissue is thus an excellent source of postsynaptic membrane proteins.

Twelve pure proteins were isolated from the dried venom of *B. multicinctus* by molecular sieving on 'Sephadex G-50' and cation-exchange chromatography on 'CM-Sephadex' (Miledi and Potter, unpublished). Four, including α-BuTX, blocked the action of acetylcholine on neuromuscular junctions in the frog sartorius; six blocked transmitter release from the motor nerves; one was acetylcholinesterase (AChE), and one was inactive at these junctions. To measure small amounts of bound toxin, the pure protein was labelled[8] with carrier-free ^{131}I at initial specific activities of 23,000 Ci/mol (8,000*g*) of toxin.

As at other cholinergic synapses, the nerve terminals to electroplaques release acetylcholine in multimolecular packages, and these "quanta" react with receptors in the postsynaptic membrane, evoking miniature synaptic potentials (Fig. 1). These potentials were used to examine the action of α-BuTX on the organ. For this purpose blocks of tissue with columns 2–8 mm high were exposed to the toxin (10^{-5} to 10^{-4} g/ml.) in elasmobranch Ringer. Miniature potentials were soon abolished in the superficial electroplaques, but it required 4 days' exposure at 4° C to 10^{-4} g/ml. to abolish miniature potentials in all the plaques of blocks 5 mm thick. Toxin-blocked electroplaques had normal resting potentials, and were insensitive to acetylcholine applied ionophoretically. In contrast, pieces of tissue kept without the toxin still had miniature potentials even 6 days after isolation. Thus it seems that in the electric organ of *Torpedo*, as at neuromuscular junctions, α-BuTX acts by blocking acetylcholine receptors. D-Tubocurarine (10^{-4} g/ml.) also abolished miniature synaptic potentials, and it required about 2 days to affect deep electroplaques. It is interesting to note that even massive injections of curare to the fish, including intra-arterial administrations, are known to act slowly in this tissue[9–11].

Because of the difficulty of applying the toxin to cells in intact tissue, subsequent studies were carried out with disrupted cells. Preliminary experiments indicated that postsynaptic membranes (identified by their content of AChE) could not be cleanly isolated from other cell membranes by density gradient centrifugation. The following procedure was therefore developed to isolate most of the total membrane content of the tissue, without large losses of AChE. Electric organs were homogenized with four times their weight of 0.4 M NaCl in a Waring blender operating at top speed for 2 min. The homogenate was poured through a sieve to remove fragments of connective tissue larger than 0.3 mm, and was centrifuged at 23,000g_{max} for 15 min. The pellet was vigorously resuspended and osmotically shocked in 20 mM sodium phosphate, *p*H 7.5 ("buffer": 1 ml./g of original tissue), with the aid of a Polytron blender operating at 22,000 r.p.m. for 1 min. This suspension was recentrifuged and the pellet was resuspended as before. Electron micrographs of the particles showed a wide range of sizes of membrane fragments and large vesicles. One gram of tissue was found to have 23.5 mg of protein[12], of which 5.6 mg, or 24% of the total, was recovered with the isolated membranes. The corresponding recovery of AChE (ref. 13) was 82% of 0.78 mmol acetylthiocholine hydrolysed per min. Assuming a molecular weight of 240,000 for the enzyme, four active sites per molecule, and an activity of 12.5 moles · acetylcholine hydrolysed per min per gram (ref. 14), there are 62 µg, and

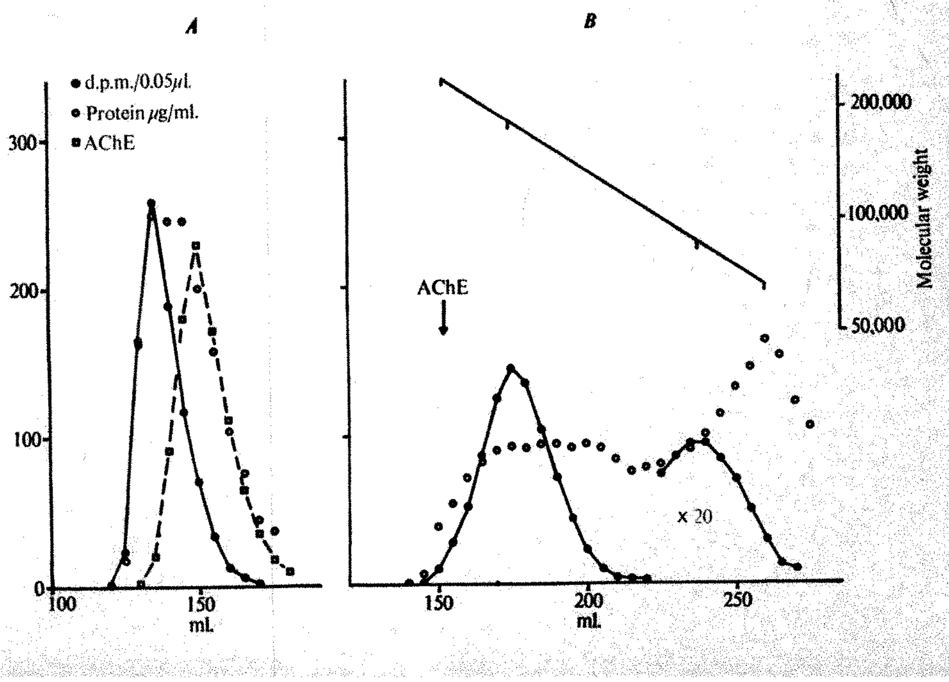

Fig. 3 Chromatography of toxin-labelled protein at 4° C on a 450 ml. column of 'Sephadex G-200' in 20 mM buffer. Membrane proteins were dissolved in 1.5% 'Triton' after partial labelling of cholinergic receptor protein on the membranes with ^{131}I-α-bungarotoxin. Results in *A* were obtained in the presence of 1.5% 'Triton'. Results in *B* were obtained with 1% 'Triton' and 0.5% SDS after the addition of 10 mg of bovine serum albumin. AChE activity is given as µmol acetylthiocholine hydrolysed/min/10 ml.; a trace of activity was noted in SDS in the position indicated. At the upper right, a plot of log molecular weight against peak elution volume between AChE (240,000) and albumin (67,000) indicates that the toxin-labelled protein moved in SDS as would globular proteins having molecular weights of about 180,000 and 88,000.

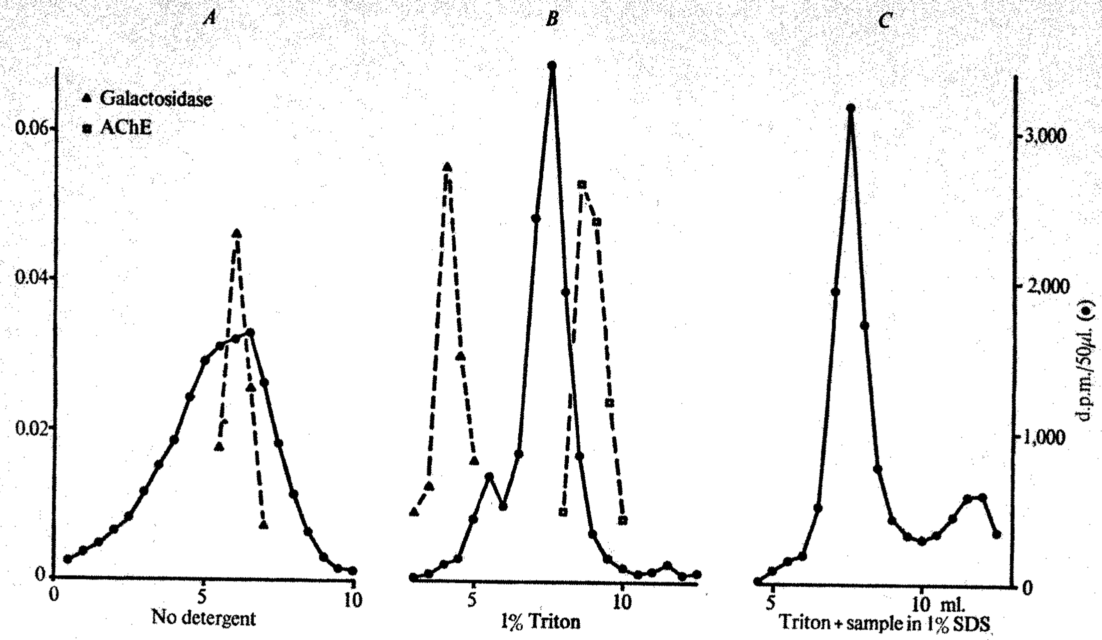

Fig. 4 Ultracentrifugation of toxin-labelled protein. Samples from the peak fraction of 'Sephadex G-200' in 1.5% 'Triton' (Fig. 3*A*) were diluted to 0.5 ml. with 50 mM Tris-HCl, *p*H 8, in 50 mM KCl–0.1 mM EDTA, and a small amount of β-galactosidase was added where indicated. The samples were centrifuged into linear density gradients of glycerol prepared in the same solution (12 ml., 10–30% glycerol v/v, in Spinco SW 40 Ti tubes), at 3° C for 15 h at 37,000 r.p.m. (*A*) or for 22 h at 39,000 r.p.m. (*B* and *C*). AChE activity is given as µmol of acetylthiocholine hydrolysed/min/ml., and β-galactosidase activity is the change in absorbance at 420 nm/min when 20 µl. of the gradient solution was added to 3 ml. of 2 mM *o*-nitrophenyl-β-D-galactopyranoside in 100 mM sodium phosphate, *p*H 7.5. The horizontal scales show the number of millilitres from the bottom of each centrifuge tube.

6.3×10^{14} active sites of AChE per gram of tissue. When 5 µg of ^{131}I-α-BuTX was added to homogenates of 1 g of tissue, the recovery of ^{131}I in the final membrane suspension was 85%.

Binding of the labelled toxin to isolated membranes was found to be dependent on the concentration of the toxin and on time, and was saturable. When the membranes from 1 g of tissue were exposed to 200 µg of toxin in 10 ml. of buffer at 4° C, the amount of toxin remaining bound to twice washed membranes (washed by sedimentation and resuspension in fresh buffer) was 7·43 µg, whether the exposure was for 1 min or 1 h. Allowing for 85% recovery of the toxin binding sites of the tissue, in the membrane suspension, there seem to be $6{\cdot}6 \times 10^{14}$ binding sites per gram of tissue. This corresponds to $5{\cdot}0 \times 10^{10}$ sites per cell (the small cells measured), and to roughly 10,000 sites/µm^2 of postsynaptic membrane. Binding of the toxin was slowed by d-tubocurarine, a competitive antagonist of acetylcholine at the receptors, and was slowed by carbamylcholine (Fig. 2). The rate of binding of the toxin also seems to be reduced at neuromuscular junctions which have been desensitized by acetylcholine (Miledi and Potter, unpublished), suggesting that the toxin does not bind effectively to desensitized receptors. This may explain the more pronounced effect of carbamylcholine than d-tubocurarine seen in Fig. 2. Carbamylcholine slowed binding of the toxin to the solubilized receptor protein (discussed later) to a similar degree, for example, by 50% in 10 min with 2×10^{-4} M carbamylcholine. Neither physostigmine, 10^{-4} M, nor 1% sodium dodecyl sulphate (SDS) had any observable effect on the amount of binding in 10 min. For these latter experiments excess labelled toxin was separated from the toxin–receptor complex on 1 ml. columns of 'Sephadex G-50'.

Several means for dissolving membrane proteins were investigated. Some partially (2 M NaBr) or fully (8 M urea) dissociated the toxin from the receptor, and others (including 2 M NaI) prevented subsequent binding of the toxin to dialysed, soluble proteins. The non-ionic detergent, 'Triton X-100', proved most satisfactory in that it quantitatively dissolved the receptor or receptor–toxin complex and AChE, and permitted the same amount of binding of the toxin to the soluble receptor as was seen with the membranes. For the following experiments the membrane-bound receptor was partially labelled with ^{131}I-α-BuTX, dissolved in 1.5% 'Triton' (w/w in buffer; 30 min at 4° C), and remaining membrane material was removed by centrifugation at 100,000*g* for 1 h. Soluble membrane proteins averaged 8% of the tissue protein.

The toxin-tagged protein was characterized as follows. On 'Sephadex G-200' (Fig. 3*A*) it was eluted in the void volume, accompanied by about 20% of the soluble membrane protein, and before AChE, indicating a molecular weight greater than that of the esterase. In contrast, when the sample and column contained SDS, the labelled protein moved in two peaks as would globular proteins having molecular weights of about 88,000 and 180,000 (Fig. 3*B*).

Ultracentrifugation in density gradients containing 1% 'Triton' showed that the toxin-labelled protein sedimented primarily in one peak (Fig. 4*B*) between the smaller marker, AChE, and a polymer of β-galactosidase from *E. coli* known to have a molecular weight of 600,000–650,000 (personal communication from P. Butterworth). Variable amounts of a somewhat larger labelled protein were always present. Without 'Triton', the labelled protein aggregated into forms which sedimented in the range 0.5–2 million (Fig. 4*A*); whereas when the toxin–receptor was pretreated with 1% SDS, and then centrifuged into a gradient containing 1% 'Triton' without SDS, both smaller units and the re-aggregated primary form were seen (Fig. 4*C*).

Preliminary studies of the binding of ^{131}I-α-BuTX to nearly pure samples of the soluble receptor protein (obtained by ultracentrifugation in 6–20% sucrose gradients containing 1% 'Triton') indicate a ratio of approximately 1 µg of toxin bound to 10 µg of protein.

From our results we can draw the following conclusions. (1) The acetylcholine receptor is a membrane-bound protein which is readily solubilized in an active state by 'Triton X-100'. (2) It is composed of units with a molecular weight of about 80,000, each of which seems to have one binding site for α-BuTX. These units aggregate into polymers, of which the primary form seen in 1% 'Triton' appears to be a tetramer having four binding sites. A hexamer would explain the somewhat larger protein. In 0.5% SDS the primary form seems to be a dimer of these units. (3) The number of toxin-binding sites per gram of tissue is the same as the number of active sites of AChE, as has been reported by others[15] for electric tissue from eels. It is interesting that if each protein has four active sites, the number of molecules of receptor and enzyme is also the same. The active enzyme and the receptor protein are clearly separable, however, and do not at present seem to have a common subunit.

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Can a Peripheral Retinal Ganglion Cell respond Differentially to Images in or out of Focus?

All modes of visual excitation are dependent on the state of focus of stimuli reaching the retina. A differential response by the ganglion cell to images in or out of focus is therefore necessary before further analysis by the visual system.

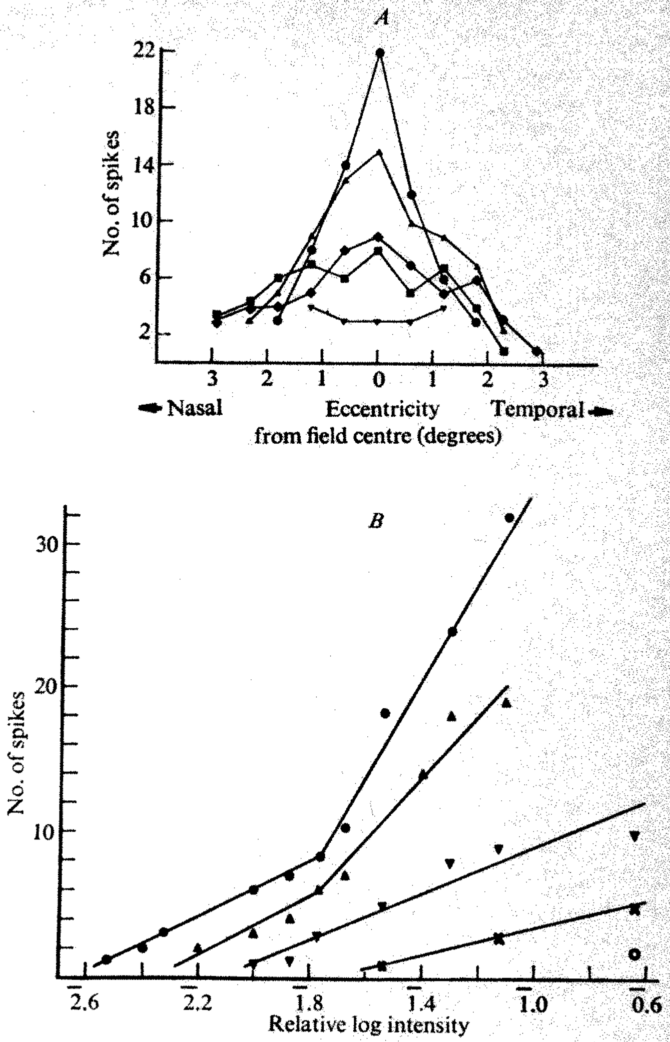

Fig. 1 *A*, Responses of a ganglion cell to a flashing spot stimulus (500 ms on/500 ms off) presented at local sites across a diameter of the receptive field when viewed through lenses of different refractive power. Although response curves were obtained for every other dioptric step from −4 to +20 dioptres, only representative curves are shown here. Corrections: ■, +16.00 dioptres; ▲, +12.00 dioptres; ●, +8.00 dioptres; ◆, +4.00 dioptres; ▼, −4.00 dioptres. *B*, Responses from the same sites as above in response to flashing (500 ms on/500 ms off) stimulus spot (28′ of the visual arc) of different intensities (log 0=45 cd m^{-2}) as viewed through a +8 dioptre lens (focused for 1 m). Background luminance=0.034 cd m^{-2}. Representative curves for nasal field sites are shown here. Curves for temporal sites are similar. Note the marked increase in sensitivity which develops at the field centre as the stimulus intensity reaches more photopic levels. ●, At field centre; ▲, 0.6° from field centre; ▼, 1.2° from field centre; ×, 2.4° from field centre; ○, 3.4° from field centre. This cell was located 34° temporal and 2° superior to the area centralis.

Of the 122 retinal ganglion cells and optic nerve fibres investigated in this study, those described were all recorded intrabulbarly following the procedure of Barlow *et al.*[1]. In order to eliminate the effect of tapetum reflexion, most of the cells were recorded from non-tapetal areas of the retina, although cells in the tapetal regions were also found to behave in a similar manner to those in non-tapetal areas. Fourteen cats (average body weight 2.8 kg) were used. The animals were surgically prepared under an initial dose of 60 mg/kg thiopentone sodium BP 2.5% solution given intraperitoneally. During the experimental period (15–20 h), they were maintained on a mixture of gallamine triethiodide (5 mg kg^{-1} h^{-1}) and thiopentone sodium (1.5 mg kg^{-1} h^{-1}) in 5% dextrose–normal saline infused by a femoral vein cannulation at a rate of 5 ml. kg^{-1} h^{-1}. They were artificially respirated with a mixture of 95% oxygen and 5% carbon dioxide. The electrocardiogram and body temperature were monitored throughout. Tungsten micro-electrodes coated with a clear vinyl lacquer (tip size 0.5 μm or less) were used in conjunction with a conventional recording system. The pupils were maintained at a diameter of 10 mm with 10% phenylephrine hydrochloride (BPC) and 0.6% atropine sulphate. The eye was fitted with a contact lens (12 mm in diameter) and was refracted along the axis of each receptive field by ophthalmoscopy and also retinoscopy. Further ophthalmic lenses were placed 12 mm in front of the eye concentric with each field axis to make the retina conjugate with the stimulus projection screen 1 metre from the eye, or to create selected degrees of refractive error. The stimulating light was projected upon the illuminated screen by the system described by Crawford and Ikeda[2]. The combination of an eye ring sutured to the sclera and continuous infusion of gallamine triethiodide ('Flaxedil') stabilized the eye. Thus, the accommodative oscillations and micronystagmus normally in play are absent in our experimental conditions.

For each cell, the boundaries and the response geometry of the receptive field were plotted with the eye corrected for one metre. A photopic test spot (28′ of the visual arc, 154.4 cd m^{-2}, 500 ms duration at 1 c.p.s.) was used as a standard for this

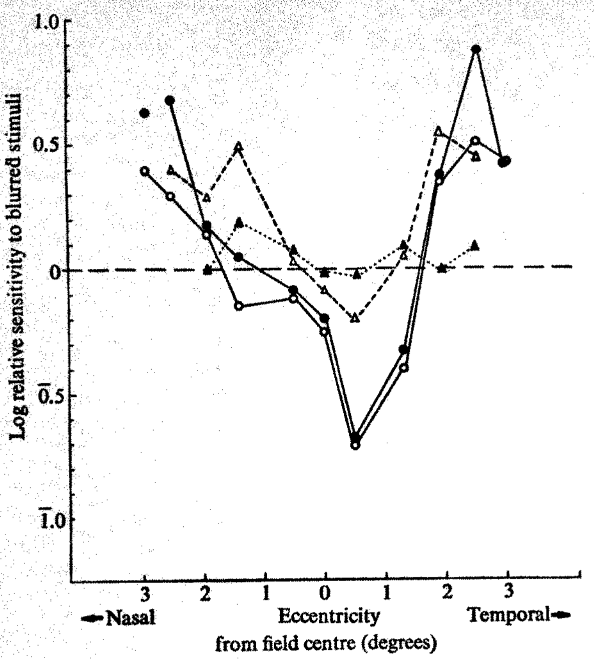

Fig. 2 Sensitivity at each of the field sites tested in Fig. 1*A*. The spike numbers were obtained with the standard spot intensity (4.802 cd m^{-2}) and with various blurring lenses in place, equated in each case with that focused stimulus intensity found for each site to produce the same spike number in Fig. 1*B*. Log 0 on the sensitivity scale is equated to 4.802 cd m^{-2} of focused stimulus intensity. The correction value given for each lens is its dioptric difference from the lens of best focus for 1 m (+8 dioptres). Only four representative curves out of thirteen obtained across the dioptric range explored (corrections from −12 to +12 dioptres) are shown here. Blurring corrections: ○, +10 dioptres; △, +4 dioptres; ▲, −2 dioptres; ●, −6 dioptres.

procedure against a background producing high contrast (0.034 cd m^{-2}). Local sites across the longest diameter of the receptive field were then replotted repeatedly and the spikes counted for each stimulation period. In the first condition, lenses of a range of refractive powers were used together with a test spot of reduced intensity (usually 1–1.5 log units below the 154.4 cd m^{-2} initially used), so that lateral interaction and light scatter would be negligible. Although we did not include the data in this communication, we have taken a series of retinal fundus photographs of the stimulus spot projected on the retina under focused and defocused conditions. The densitometer analysis of such photographs indicated that the light scatter is negligible (5% of the diameter of the spot of the retina). In the second, a wide range of spot intensities was used (usually a 3 log unit range) with the best refractive correction in place. This procedure made it necessary to record from a ganglion cell for 4–5 h. Fig. 1 shows a representative result obtained from a ganglion cell located in the peripheral retina whose receptive field projects into visual space, 34° nasal and 2° inferior to the visual axis. The cell responded vigorously to light "on" throughout the receptive field and only sporadically to light "off" at the field periphery, even in high contrast stimulus conditions and at photopic background levels.

In Fig. 1*A*, the number of spikes produced with the test light "on" at each location along the horizontal axis within the receptive field is shown for representative refractive conditions. To determine local thresholds without lateral interaction, a stimulus condition which evoked no "off" response was chosen. In Fig. 1*B*, the spike count as a function of log intensity of the stimulus spot is shown for each of those sites tested across the receptive field of the ganglion cell in the focused conditions. The relative sensitivity at each test site to focused compared with defocused stimuli was then determined by finding the focused test spot intensity from Fig. 1*B* which produced the same spike count as a given blurred stimulus at that site (Fig. 1*A*). The values for all sites tested are summarized in Fig. 2.

For focused images the threshold increases steeply away from the centre of the receptive field. The response is sensitive to changes of 15′ of an arc or less, suggesting a critical centre favouring a directional mechanism even for visual fields 30° or more from the visual axis (see Fig. 1*A*, +8 DS curve).

Although out of focus stimuli of 28′ of an arc or less may remain detectable over a considerable dioptic range (upward of ±12 dioptres for the conditions used), directionalization based on the slope of the spike–distance curve deteriorates rapidly (see Fig. 1*A*, +12 and +4 DS curves). In extreme defocused conditions, the local thresholds may become so uniform across the field that the same spike number may be produced for a given stimulus anywhere within the receptive field (see Fig. 1*A*, +16 and −4 DS curves), thus permitting the maximal directional error in space (that is, equal to the radius of the field).

In defocused conditions, the cell responds rather more robustly to the stimulus when it is presented at the periphery of the receptive field than under the focused conditions; no light produces no response at all. Thus an apparent increase in peripheral sensitivity seems to occur (Fig. 2). Although the directional role of the cell is considerably diminished, it continues to detect quite effectively the presence of the diffuse image (see Fig. 1*A*, −4 DS curves).

The peripheral ganglion cell thus combines a large receptive field for the detection of diffuse images with a central organization favouring the localization of sharp images.

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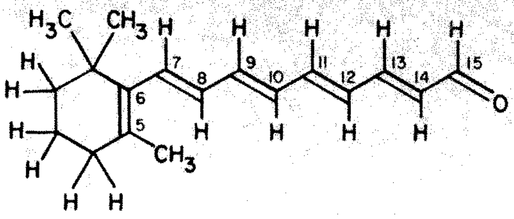
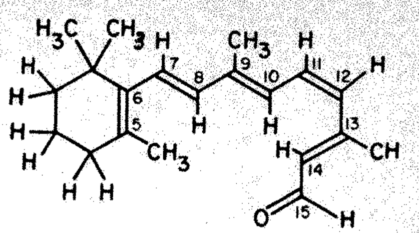
Implications of Torsional Potential of Retinal Isomers for Visual Excitation

BECAUSE 11-*cis* retinal is the chromophore of the visual pigment in vertebrate rods, and its isomerization to the all-*trans* form (I*a*) is known to occur during visual excitation[1–4], the properties of the retinal isomers are of considerable interest. Although it has long been assumed that non-bonded repulsions in 11-*cis* retinal distort the polyene chain, the details of the ground state geometry have not been determined, nor has the experimental spectrum been correlated unequivocally with the excited states. In this communication, we present a theoretical ground state potential function with a form which may help to explain some of the unusual spectral characteristics of the retinal isomers when in solution or incorporated into the native visual pigment[1–4].

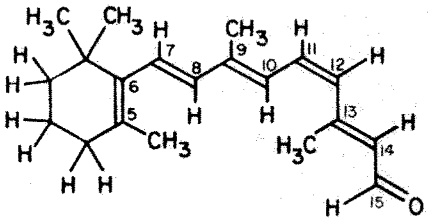
Fig. 1 shows the calculated potential energy of 11-*cis* retinal as a function of the C_{12}—C_{13} torsional angle; the method is outlined in the figure caption[5–10]. A conformation in which the C_{12}—C_{13} bond is twisted by approximately 130° from the



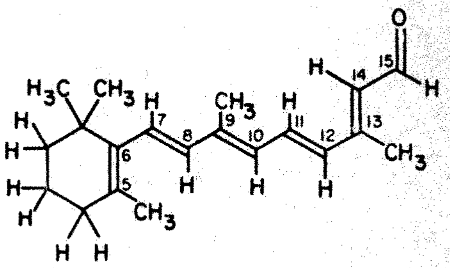
(a) all-trans



(b) 11-cis, 12-s-cis



(c) 11-cis, 12-s-trans



(d) 11-trans, 12-s-cis

planar s-*trans* geometry (that is, a distorted s-*cis* conformation, (*b*)) is slightly more stable than the distorted s-*trans* conformation (60° from planar s-*trans*, (*c*)) that has been assumed in all previous discussions of 11-*cis* retinal[1-4,6]. Of course, the quantitative energy differences are not significant and the exact shape of the curve depends on the parameter values (for example, distorted s-*trans* can be slightly more stable than distorted s-*cis*), but the qualitative conclusion that 11-*cis* retinal has a relatively broad and flat minimum is certain to be valid. Thus, the essential difference between the all-*trans* and the hindered 11-*cis* compound, both of which are expected to have 12-s-*cis* conformations with energies similar to 12-s-*trans*, is that in 11-*cis* retinal the s-*trans* and s-*cis* minima are much nearer to 90° (s-*trans*, 60°; s-*cis*, 130°) and have a much lower barrier between them than in all-*trans* retinal.

The torsion around C_{11}—C_{12}, which has been emphasized before[3,11,12], is relatively small in 11-*cis* retinal (Table 1).

Definitive experimental information on the geometry of 11-*cis* retinal is not available. A recent nuclear magnetic resonance study[13] of several isomers, including the 11-*cis* compound, gives qualitative results in agreement with the calculated potential energy surface, although the data do not distinguish between the s-*cis* and s-*trans* conformation about the C_{12}—C_{13} bond.

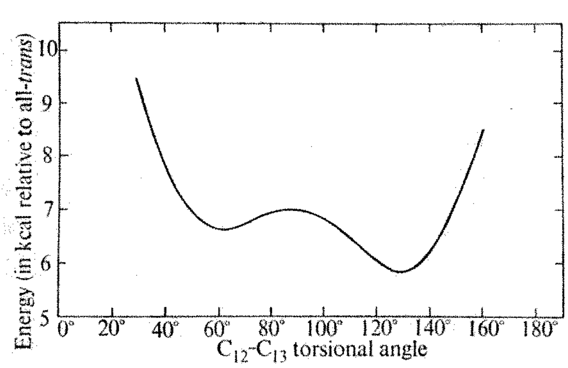


Fig. 1 Potential function for rotation of 11-*cis* retinal about C_{12}—C_{13}; $\theta = 0°$ corresponds to the s-*trans* linkage. At each point on the curve, the energy $E^{\pi} + E^{nb}$, where E^{π} is the Hückel π-electron energy and E^{nb} is a pairwise sum over nonbonded interactions, was minimized with respect to rotation about C_{10}—C_{11} and C_{12}—C_{13}; all bond lengths and angles were kept fixed at standard values (C_6—C_7 angle is 135°); nonbonded parameters were from ref. 5, except that a point methyl group was used to simulate free rotation.

It is interesting to consider the spectral consequences of the potential surface shown in Fig. 1. The calculated energy ΔE (eV) and frequency $\tilde{\nu}$ (cm^{-1}) of the lowest $\pi \rightarrow \pi^*$ transition for a series of geometries corresponding to Fig. 1 are listed in columns five and six of Table 1. It is clear that, in the neighbourhood of the minimum energy conformation, there occurs nothing like the complete "break" in conjugation postulated by some workers[14]. Values of $\Delta\tilde{\nu}$ (cm^{-1}), the frequency relative to that calculated for the all-*trans* compound, are given in column seven of Table 1. Because "vertical" transition frequencies were calculated for each ground state geometry, the shifts approximate those of the absorption band maxima. The experimental maxima in the room temperature absorption spectra of all-*trans* and 11-*cis* retinal dissolved in hexane are 27,174 cm^{-1} and 27,397 cm^{-1}, respectively[4].

Table 1 Energies and Spectra of Retinal as a Function of Geometry

Torsional angles*						
C_{12}—C_{13}	C_{10}—C_{11}	C_{11}—C_{12}	E_0 (kcalories)†	ΔE (eV)	$\tilde{\nu}$ (cm^{-1})	$\Delta\tilde{\nu}$ (cm^{-1})‡
0°	0°	0°	0	3.66	29,520	0
180	0	0	1.77	3.54	28,553	−967
0	0	180	—	3.63	29,279	−241
180	0	180	—	3.52	28,391	−1,129
30	20	200	9.30	3.69	29,763	243
40	20	195	7.75	3.79	30,569	1,049
50	20	190	6.85	3.89	31,376	1,856
60	10	190	6.58	3.95	31,860	2,340
90	0	180	6.90	4.12	33,231	3,711
120	−15	175	5.90	3.93	31,698	2,178
130	−10	170	5.75	3.79	30,569	1,049
140	−10	165	6.15	3.66	29,521	0
150	−15	160	7.0	3.54	28,553	−967

The various geometries are determined as indicated in the text and the legend to Fig. 1; the excitation energies were obtained by a Pariser–Parr–Pople SCF-CI calculation with a modified version of a program from the Quantum Chemistry Program Exchange (Program No. 71.2).

* The listed angles are relative to *trans* as zero and are rounded to 5° because a more precise value is not justified by the calculation; the C_6—C_7 angle is taken to be 135°.

† E_0 is the ground state energy relative to that of planar all-*trans* retinal.

‡ $\tilde{\nu}$ of the particular conformation minus $\tilde{\nu}$ of all-*trans* retinal.

What is striking about these values[4,15,16] is that the 11-*cis* maximum is shifted by only 223 cm^{-1} relative to the all-*trans* compound. For a molecule like 11-*cis* retinal, in which steric repulsion leads to a ground state geometry that is twisted primarily about single bonds, a shift to significantly shorter wavelengths is expected because the energy of the π^* orbital is raised relative to that of the π orbital. Such high frequency shifts ($\lesssim 2,000$ cm^{-1}), which result in part from variation in vibrational overlap, have been observed in hindered *cis* compounds[15-17]. Table 1 shows that at the s-*trans* minimum ($\sphericalangle[C_{12}—C_{13}] \simeq 60°$) the frequency is displaced by 2,340 cm^{-1} from that of all-*trans* retinal, while at the s-*cis* minimum ($\sphericalangle[C_{12}=C_{13}] \simeq 130°$) the shift is only 1,049 cm^{-1}; it is reduced to zero for $\sphericalangle[C_{12}—C_{13}] \simeq 140°$. To obtain no shift for s-*trans* requires an angle of less than 30°, a highly unstable ground state conformation (Table 1). Comparison of the results for the planar form of 11-*cis* retinal (s-*trans*, $\Delta\tilde{\nu} = -241$ cm^{-1}; s-*cis*, $\Delta\tilde{\nu} = -1,129$ cm^{-1}) demonstrates that the calculated effect is an s-*cis* "redshift" well known in polyene chemistry[18,19].

The potential energy curve in Fig. 1 suggests an explanation for the anomalous temperature dependence of the spectrum of 11-*cis* retinal and other hindered polyene isomers[15,16]. At room temperature the molecule would be expected to undergo transitions from vibrational levels with contributions from a wide range of geometries in the neighbourhood of the s-*trans* as well as the s-*cis* minimum. There would clearly result a broad absorption peak, which could become significantly narrower and more intense at lower temperatures when the molecule is "trapped" in the appropriate minimum energy conformation.

The 11,13-*dicis* isomer of retinal is considerably less stable and has its principal absorption peak at a significantly shorter wavelength than the 11-*cis* isomer[20]. Both of these results can be understood if 11-*cis* is s-*cis* about $C_{12}—C_{13}$, and 11,13-*dicis* is a more highly hindered s-*cis* compound or, alternatively, forced into the s-*trans* configuration.

If 11-*cis*, 12-s-*cis* retinal were the chromophore present in the visual system, the initial photoproduct resulting from the isomerization would be a molecule that is *trans* about the $C_{11}—C_{12}$ double bond but remains s-*cis* about $C_{12}—C_{13}$, as the $C_{12}—C_{13}$ bond has more double bond character in the π^* excited state. Because the resulting 11-*trans*, 12-s-*cis* isomer would be essentially planar (without distortion by the lipoprotein), a large redshift due to the s-*cis* conformation is expected; the calculated values are $-2,016$ cm^{-1} relative to the distorted 11-*cis*, 12-s-*trans* retinal and -970 cm^{-1} relative to the planar all-*trans* compound. The ground state planar 11-*trans*, 12-s-*cis* can isomerize thermally to all-*trans* retinal; the calculated barrier is 4 kcalories. The series of reactions

$$\underset{(\mathrm{I}b)}{\text{11-}cis\text{, 12-s-}cis} \xrightarrow{h\nu} \underset{(\mathrm{I}d)}{\text{11-}trans\text{, 12-s-}cis} \xrightarrow{\text{thermal}} \underset{(\mathrm{I}a)}{\text{11-}cis\text{, 12-s-}trans}$$

would correspond to the observed changes in the visual pigment spectrum that are associated with the transformations[1]

$$\text{rhodopsin} \xrightarrow{h\nu} \text{prelumirhodopsin} \xrightarrow{\text{thermal}} \text{lumirhodopsin}$$

in which the intermediate, prelumirhodopsin, is strongly redshifted ($-1,680$ cm^{-1}) relative to rhodopsin and lumirhodopsin, which have similar absorption maxima. That these steps in the rhodopsin cycle are primarily alterations in the chromophore and do not involve significant conformational changes in the lipoprotein complex is in agreement with thermodynamic measurements[1,2,21,22].

It is clear that the general features of the torsional potential described in this report must play an important part in the properties of 11-*cis* retinal and other "hindered" *cis* isomers of conjugated systems. The validity of the specific proposals concerning the possible forms of the early intermediates in the visual cycle is far less certain. We have included them primarily as a possible focus for further conformational studies of these molecules. Details of the calculations, including an interpretation of the shape and temperature dependence of the various absorption bands, will be reported in subsequent publications.

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Role of the Pericorneal Papillary Structure in Renewal of Corneal Epithelium

THE human cornea is covered by a five-layered epithelium. Cells are continually shed from its surface and replaced by division of the basal cells, which has a mean generation time estimated to be about 4 days[1]. Because of the papillae in the skin, the relation between the area of the basal cell layer and the surface is about 20 : 1. Because it must be refractive, there can be no papillae on the cornea, and the relation between the basal cell layer and the surface is accordingly 1 : 1. This should correspond to higher demands on the generative capacity of the corneal basal cells compared with skin. The epidermal basal cells are in close contact with a well developed capillary network. There are no vessels in the cornea, and so it can be assumed that the supply of its epithelium is poorer. Corneal epithelium, nonetheless, has considerable healing capacity, which is achieved primarily by migration of epithelial cells.

An interesting possibility concerning the renewal of corneal epithelial cells is suggested by study of the transitional zone between cornea and conjunctiva, that is, the limbus corneae. Here the so-called palisades of Vogt are found: fine radial lines about 1 mm long and four per mm of the corneal circumference. Their anatomy and function have given rise to controversy since, in 1859, Manz described limbal epithelial structures in swine, which were thought to be glands. Aurell and Kornerup[2] concluded that the glands of Manz were rudiments of accessory limbal lachrymal glands. Duke-Elder[3,4] considered the limbal structures in man to be functionless vestigial traces of the glands of Manz. The limbal palisades consist of subepithelial, richly vascularized papillae (Fig. 1) between which the epithelium projects downwards in radial ridge-like thickenings filling the interstices between the papillae. The palisades are particularly striking in negroes, because the limbal pigment contains melanin, which is seen in thick layer in the epithelial depressions. The radial pigmented lines are sometimes very thin and delicate, and arranged in pairs. This is because the melanin may be concentrated in the basal cell layer, which is directed vertically in relation to the surface along both sides of the papillary crests. It is tempting to suppose that this distinct structure fulfils a purpose.

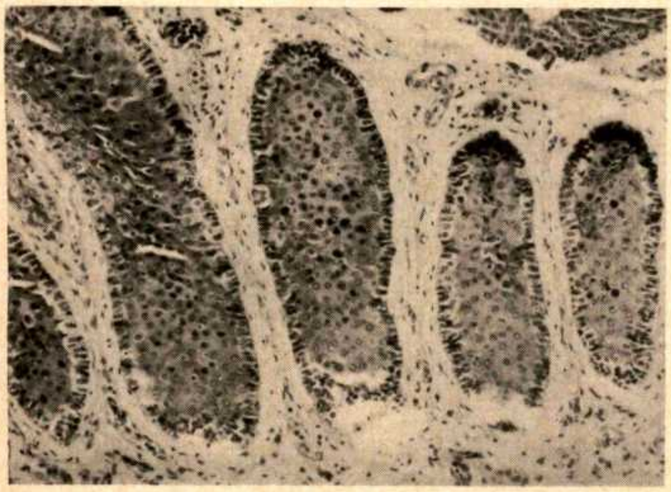

Fig. 1 The papillary limbal structure, the palisades of Vogt. This section, from a negro, is parallel with the limbal surface.

Our theory is that the limbal papillary structure serves as a generative organ for corneal epithelial cells. The generative capacity of the basal cell layer of cornea proper is thought to be insufficient to meet the loss of cells from the surface. To compensate for the deficit, a part of the generative cell population is placed at limbus, where the basal cell layer is large relative to the surface, and is adjacent to a well developed net of capillaries. This would preserve the transparency and refractive properties of the cornea.

The most direct evidence that the limbal structure can produce cells that migrate over the cornea is that if the epithelium is removed from the whole corneal surface, a normal epithelial cover redevelops after some days. The source of these cells must be the epithelial depressions between the limbal papillae.

This is supported by the following experiment. The epithelium was removed in an area adjacent to the pigmented limbal ring in a guinea-pig. Twenty-four hours later the erosion had been covered over with epithelium. This was pigmented over most of the erosion area, and the limbal pigment was lighter in the corresponding area. Five days later the corneal pigmentation had disappeared and the limbal pigmentation was normal. Furthermore, a significantly higher count of colcemid-arrested mitoses was found in the limbal structure of a guinea-pig's eye in which a central corneal erosion had been made 24 h earlier than in the other eye.

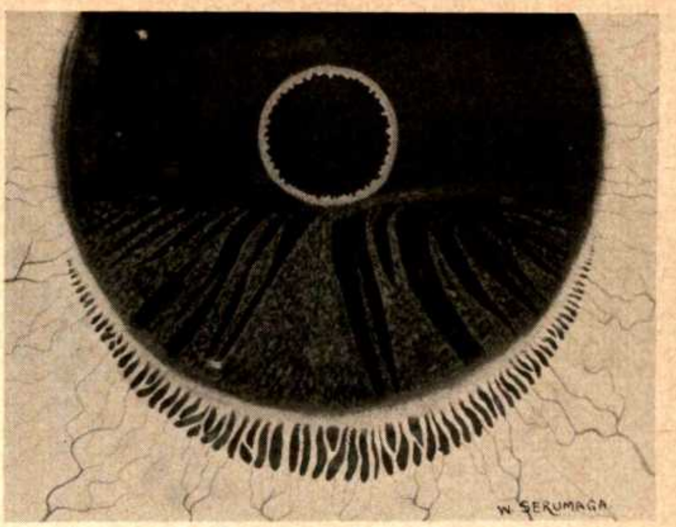

Fig. 2 The limbal and corneal pigmentation in a negro.

The pattern illustrated in Fig. 2 could be explained by migration from the limbus in normal circumstances. The cells are arranged along lines arcuating from the limbal basal cells towards the cornea. The assumption of a physiological migration of cells is further supported by, and explains, the pigmented lines which curve in over the cornea from the pigmented limbal ring in negro eyes. The melanin is contained in the superficial epithelial cells, whereas the underlying basal cells are not pigmented. The pigmented lines are thought to indicate the direction of migration. These lines are best developed from the inferior limbus, from which they may curve horizontally and come together at a Hudson–Staehli's line. It is thought that this line indicates a borderline of cell migration from the inferior limbus.

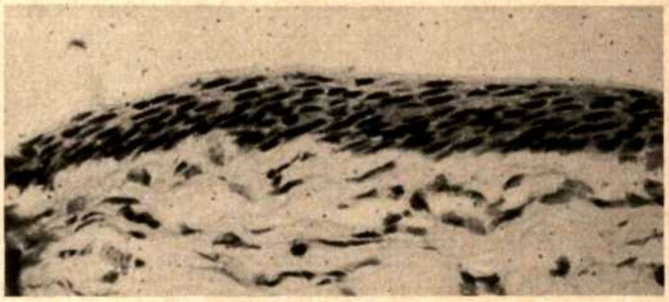

Fig. 3 Radial section through limbus corneae, vertical in relation to the corneal surface (guinea-pig).

A failure in the limbal structure may be the cause of pterygium, a condition in which the corneal surface is invaded by conjunctival tissue. The primary lesion in keratoconus consists of degenerative processes in the basal epithelial cells. These may be caused by a failure in the renewal of the epithelium from the limbal papillary structure.

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Conjecture on the Visual Estimation of Relative Radial Motion

THE ability to estimate accurately the time interval until the juncture of an observer with an object moving with relative radial velocity towards the observer seems to be highly developed in humans and many animals. In many practical situations, of probable importance for survival, it is not the distance of the object from the observer which is of interest, nor is it the velocity of the object, but rather the ratio of the two, which gives the time taken by the object to reach the observer. The importance of this parameter has certainly been renewed in the age of the motor car. The popularity of ball games may be partly due to the exercise of this faculty otherwise dormant in a sedentary era.

I wish to show here that there is sufficient information available on the monocular retina to allow the observer to estimate the time of juncture with the moving object without the need for absolute knowledge of the distance of the object, its size or its velocity.

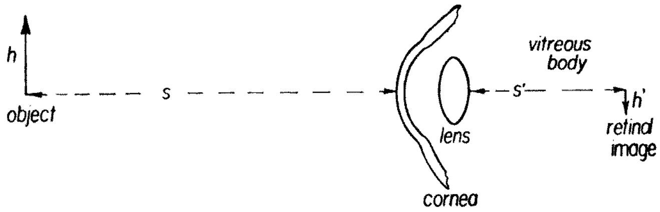

Fig. 1 Optical system of the eye of the observer and an object moving with uniform radial velocity towards the observer (not to scale).

Fig. 1 shows schematically an optical system representing the eye of the observer and an object of size h at a distance S from the observer. If v is the relative uniform velocity of the object towards the observer then the time interval until juncture is given by

$$t = \frac{S}{v} \tag{1}$$

For paraxial rays Lagrange's law gives for the image size h' on the retina

$$h' = \frac{h}{S} \frac{S'}{n'} \tag{2}$$

where S' is the distance of the retina from the lens and n' the index of refraction of the vitreous humour.

Differentiating equation (2) with respect to time gives

$$\frac{dh'}{dt} = -\frac{dS}{dt} \frac{hS'}{S^2 n'} = v \frac{hS'}{S^2 n'} \tag{3}$$

because S' may be assumed constant.

Dividing equation (2) by equation (3) gives

$$\frac{h'}{\frac{dh'}{dt}} = \frac{S}{v} = t \tag{4}$$

that is, the time interval of interest.

Thus a knowledge of the instantaneous image size and its time derivative is sufficient to determine, with monocular vision alone, the juncture interval without requiring absolute knowledge of S, v or even h.

The verification of the conjecture that the visual system is sufficiently adept to estimate the time interval to juncture from the limited but sufficient retinal information is an interesting experimental problem.

Commenting on this conjecture, Professor R. L. Gregory (private communication) has remarked: "Visual size is not, of course, merely a matter of retinal size and it is not very clear how the information of the retinal size is retained after 'constancy scaling'. This itself is an interesting question and I would like to know the answer."

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Changes in Adrenal Enzymes synthesizing Catecholamines in Attack Behaviour evoked by Hypothalamic Stimulation in the Cat

IN the cat, electrical stimulation[1,2] or selective lesions of the brain[3] can evoke an affected display of anger, called sham rage[3]. This emotional display is often coupled with directed prey killing or attack behaviour[2]. Associated with this is a widespread activation of the sympathetic nervous system and a release of the catecholamines, noradrenaline and adrenaline, from the adrenal gland[4,5]. It was recently demonstrated that, when prolonged, increased neural release of adrenal catecholamines is associated with increased activity of tyrosine hydroxylase[6,7], the enzyme of the rate-limiting step in catecholamine biosynthesis[8]. The increase in enzyme activity is presumably the result of production of new enzyme[6,9]. We have sought to determine whether the induction of attack behaviour in the cat by electrical stimulation of the hypothalamus, if sustained over several days, can lead to similar changes in adrenal tyrosine hydroxylase and also the adrenal enzyme phenylethenol amine-N-methyl transferase (PNMT) which converts norepinephrine to epinephrine.

In a preliminary operation, adult cats were placed under halothane anaesthesia and electrode guides were stereotactically placed through drill holes in the calvarium, over sites in the posterior hypothalamus from which attack behaviour can be evoked[2]. Several days later the animals were placed in an observation cage with an anaesthetized rat and an insulated monopolar electrode with a 0.5 mm bare tip was lowered and fixed into the locus at which rat-killing behaviour could be evoked by electrical stimulation. The anode was a screw embedded in the skull. In controls, the electrode was placed in immediately adjacent hypothalamic regions from which some motor activity but not rage or prey-killing could be elicited. Animals were electrically stimulated from a constant current stimulator for 90 min in the morning and in the afternoon for 3 consecutive days. The stimulus programme consisted of 2 min trains of square wave pulses (0.5 ms duration, 0.5–2.0 mA, 70 c.p.s.) each followed by a 3 min rest. After the last stimulation session, the animals were lightly anaesthetized with

Table 1 Enzyme Activity in Adrenal Gland after Brain Stimulation

	Tyrosine hydroxylase*	PNMT*
Control	93.8 ± 9.6	14.1 ± 1.7
(n)	(13)	(13)
3 day stimulation,	157 ± 34.3	13.7 ± 2.0
no attack	(10)	(10)
(n)	NS	NS
3 day stimulation,	412 ± 44.6†	30.4 ± 2.1†
attack	(10)	(12)
(n)		

* Activity expressed by nmol of product/100 mg/20 min ± s.e.m.
† Difference from control significant ($P < 0.001$).
NS, Difference from control not significant ($P > 0.05$).

Table 2 Effects of Unilateral Adrenal Denervation on Enzyme Activity of Adrenal Gland after Brain Stimulation

	Tyrosine hydroxylase*		PNMT*	
	R	*L* (denervated)	*R*	*L* (denervated)
Control	84±9.0	105±17	11.7±13	10.3±0.7
(n)	(7)	(6)	(7)	(6)
3 day stimulation, no attack	179±50	112±35	14.7±3.9	9.1±3.4
(n)	(3)	(3)	(3)	(3)
Change from control	NS	NS	NS	NS
3 day stimulation, attack	257±18	112±12†	18.7±2.1	11.8±1.6‡
(n)	(6)	(6)	(6)	(6)
Change from control	<0.001	NS	<0.02	NS

* Activity expressed as nmol of product/100 mg/20 min ±s.e.m.
† Difference from right gland significant ($P<0.001$).
‡ Difference from right gland significant ($P<0.02$).
NS, Not significant.

chloroform, killed by decapitation, and the adrenal glands removed and frozen in dry ice.

The adrenal glands were weighed, homogenized in 4 volumes of 0.25 M sucrose and centrifuged to remove debris. The supernatants were recentrifuged at 100,000*g* to spin out the microsomal fraction and then dialysed. Enzyme activity[10] was assayed by end-product inhibition. The pellet from high speed centrifugation of the adrenal gland was re-homogenized in 0.02 M K_2PO_4 buffer (*p*H 6.5) and aliquots were taken to assay tyrosine hydroxylase by the method of Nagatsu *et al.*[10] and PNMT by the method of Axelrod[11]. No differences in enzyme activities were found between the right and left adrenal glands.

Changes in the activity of adrenal tyrosine hydroxylase and PNMT can be seen in Table 1. After 3 days of stimulation producing attack behaviour the tyrosine hydroxylase activity increased to four times the original value and PNMT activity doubled. In stimulated controls there was no change in enzyme activity.

To determine whether the increased activity of adrenal tyrosine hydroxylase and PNMT depended on the neural innervation of the adrenal gland, the left adrenal gland was denervated. Changes in enzyme activity in innervated and denervated adrenals were measured in unstimulated controls, stimulated animals with attack behaviour and stimulated animals without attack behaviour (Table 2). Brain stimulation which produced attack behaviour tripled the activity of tyrosine hydroxylase and almost doubled the activity of PNMT in the innervated gland. Electrical stimulation producing alertness or movement but not attack did not cause significant changes in enzyme activity. In the denervated gland, enzyme activity did not increase. Thus the increase in activity of both adrenal enzymes after hypothalamic stimulation depends on intact innervation to the adrenal medulla and therefore probably involves efferent nerve impulses.

This study demonstrates that intermittent electrical stimulation of the hypothalamus during 3 days can lead to increased activity of tyrosine hydroxylase and PNMT in the adrenal gland. Moreover, the changes in enzyme activity seem to be behaviourally specific, for they do not occur when hypothalamic stimulation failed to evoke attack behaviour. The failure of enzyme activity to increase in the denervated adrenal gland indicates that the increase in enzyme activity depends on nerve impulses. In the adrenal gland tyrosine hydroxylase has been shown to be increased by nerve impulse activity in immobilization stress[12] and presumably after reserpine[7,13]. While increased activity of PNMT occurs after reserpine treatment, presumably through a neurogenic mechanism[13], the work described here provides the first direct evidence for a neural participation in the regulation of this important enzyme. Because nerve impulses are also necessary for the release of adrenal catecholamines in sham rage[4,5] it is possible that the amines themselves play a part in regulating the rate of enzyme synthesis.

Activation of the sympathetic nervous system and enhanced secretion of adrenal catecholamines are a common denominator in behaviour in which animals are prepared for fight or flight. This view, proposed by Cannon[14], emphasizes the utility of catecholamine release for the immediate physiological adaptation of visceral and metabolic activity to the emotional arousal. The present study adds another dimension to this concept. It suggests that, when sustained, behaviour characterized by sympathetic and adrenomedullary hyperactivity can lead to changes in enzymes involved in the synthesis of the transmitters themselves. The changes seem to increase the availability of catecholamines at receptors by increasing the activity of critical enzymatic steps essential for synthesis. The consequences of these changes for long range behavioural and visceral control, however, remain to be elucidated.

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Duration of *in vivo* Effects of L-Asparaginase on Experimental Metastasis

L-ASPARAGINASE has been used to treat various neoplasms in man and animals[1-4], and was at first believed to act only on malignant cells which are dependent on asparagine. Clinical investigations, however, indicated that L-asparaginase could itself be antigenic[5] and have serious side effects. Moreover, L-asparaginase has been found to lead to suppression of phytohaemagglutinin-induced blastogenesis of human lymphocytes[6-8]. Depression of the immune response to sheep red blood cells in mice treated with the enzyme has been reported[9]. Inhibition of the graft versus host reaction in rats and mice[10] as well as reduction of the immune reactivity to an allografted tumour[11] have also been observed.

The amounts of L-asparaginase necessary to produce regression of sensitive tumours have been worked out, but the frequency of administration required for optimal *in vivo* effects is not known. We report here the effects of L-asparaginase on the incidence of experimental metastasis and describe an assay to determine the duration of *in vivo* effects of a single dose of the enzyme.

B16 melanoma adapted to grow in tissue culture was used in C57BL/6J mice. *In vitro* cytotoxicity studies with various concentrations of L-asparaginase (1–50 IU/ml. media) revealed no inhibition of growth. Five groups of mice (12–14 weeks old) were injected intraperitoneally with 5,000 IU/kg of L-asparaginase (Merck, Sharp, and Dohme) each day; control groups were injected with saline. The start of treatment ranged from 3 days before to 3 days after intravenous inoculation of 50,000 B16 melanoma cells. Treatments were carried out daily until the seventh day after injection of tumour cells. Mice were killed on the fourteenth day and their lungs were removed. Pulmonary metastases were counted under a dissecting microscope. Student's *t* test was used in all evaluations of differences between means of each treatment group and its matched control. The results (Table 1) demonstrated that there were significantly more lung metastases ($P < 0.001$) in the mice treated with L-asparaginase before or on the day of tumour inoculation, compared with controls. No differences in the incidence of metastases were demonstrable between mice treated with L-asparaginase after tumour cell injection and controls.

Table 1 Incidence of Lung Metastases in Mice injected Intravenously with Melanoma Cells and treated with L-Asparaginase or Saline

	No. of lung metastases *	
Start of treatment	L-Asparaginase	Saline (control)
3 days before tumour †	176 ± 14	68 ± 9
2 days before tumour †	180 ± 17	67 ± 7
1 day before tumour †	182 ± 14	70 ± 11
Same day as tumour†	108 ± 11	62 ± 9
1 day after tumour ‡	80 ± 9	72 ± 14
2 days after tumour ‡	68 ± 6	67 ± 7
3 days after tumour ‡	69 ± 7	64 ± 6

* Mean number of lung nodules in eight animals (per group).

† Lung metastases in L-asparaginase and saline-treated animals differed significantly ($P < 0.001$).

‡ No statistical differences in the number of lung metastases were demonstrated.

We then determined the duration of the effect of a single dose of L-asparaginase on the incidence of experimental metastasis. C57 mice, divided into six treatment and control groups, received a single intraperitoneal injection of 5,000 IU/kg of L-asparaginase or of saline. Injections were given at different times, from 7 days before, to the same day as the intravenous injection of 60,000 B16 melanoma cells. Animals were killed 14 days later, and the lung metastases were counted. The results (Table 2) showed that there were significantly more lung metastases ($P < 0.001$) in mice treated once with L-asparaginase either on the same day, or 1 or 2 days before tumour cell injection, than in the controls. On the other hand, in animals treated with L-asparaginase 3 or more days before tumour cell injection there was no increase in the number of lung metastases.

Table 2 Duration of *in vivo* Effects of a Single Dose of L-Asparaginase on the Incidence of Experimental Metastasis

Single dose	No. of lung metastases *	
day of treatment	L-Asparaginase	Saline (control)
7 days before tumour †	55 ± 5	56 ± 5
5 days before tumour †	53 ± 6	60 ± 9
3 days before tumour †	50 ± 5	58 ± 6
2 days before tumour ‡	83 ± 7	52 ± 7
1 day before tumour ‡	154 ± 13	59 ± 5
Same day as tumour ‡	135 ± 14	53 ± 6

* Mean number of lung nodules in seven animals (per group).

† Comparison of L-asparaginase and saline treated animals demonstrated no difference in the number of lung metastases.

‡ The number of lung metastases in L-asparaginase and saline treated controls differed significantly ($P < 0.001$).

Thus we can conclude that L-asparaginase increases the incidence of pulmonary metastases, and that this increase may be due to host immunosuppression. Furthermore, in our system the duration of this effect after a single dose has been found to be about 48 h, so that administration of L-asparaginase to achieve immunosuppression might only be necessary every 2 or more days.

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Rapid Cell Culture Assay Technique for Murine Leukaemia Viruses

INFECTION of susceptible mouse cells in culture with murine leukaemia viruses (MLV) does not cause any observable change in cellular morphology, even though continuous virus replication in these cells can often be demonstrated. Complement-fixation[1] and fluorescent antibody[2] techniques as well as interference[3] or potentiation[4] of focus formation by "defective" murine sarcoma viruses have all been used successfully to detect and to quantitate *in vitro* infection of mouse cell cultures with MLV. These techniques, however, are less than ideal because they involve special reagents and lengthy incubation, or because they are relatively insensitive. Klement *et al.*[5] have shown that the XC cell line[6], derived from a rat

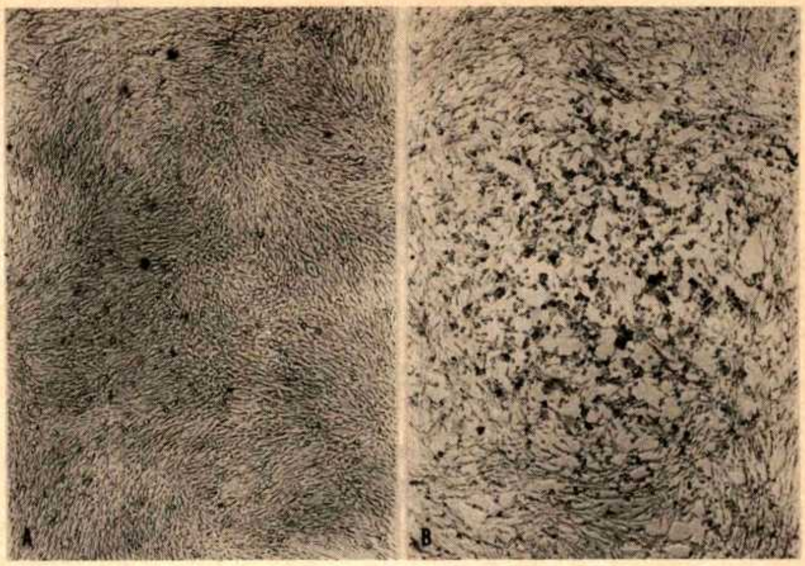

Fig. 1 *A*, Control S+L− mouse cells. *B*, Lytic focus with characteristic clusters of round cells appearing in S+L− cells 5 days after superinfection with MLV. Unstained; ×48.

tumour induced by the Prague strain of Rous sarcoma virus, undergoes syncytium formation when present in mixed cultures together with MLV-infected mouse cells. This phenomenon of mixed culture cytopathogenicity has been used to develop a plaque assay for murine leukaemia viruses in mouse cell cultures (unpublished observations of W. P. Rowe *et al.*).

During the course of our experiments, designed to study the interrelationships between "defective" murine sarcoma viruses (MSV) and MLV, we were able to isolate transformed 3T3 mouse cells which contained the MSV genome in the absence of detectable MLV[7,8]. Normal 3T3 cells were infected with dilutions of MSV and immediately plated as suspension cultures in media containing 0.3% agar. Colonies of transformed cells, proportional to the concentration of MSV used for infection, first appeared after approximately 2 weeks and increased steadily in size. Several colonies were isolated from the agar suspension plates and grown as monolayer cultures. Some of these colonies gave rise to viable cell lines which continuously released MSV into the culture medium, while other colonies yielded monolayer cultures containing MSV-transformed cells but from which no focus-forming MSV could be recovered. These latter cells, termed "sarcoma positive leukaemia negative" (S+L−), did not release detectable quantities of MSV unless superinfected with any of several strains of MLV, and seemed to contain the MSV genome in the absence of replicating leukaemia virus. One of the S+L− cell lines, in addition to releasing MSV after superinfection with MLV, responded with the formation of MSV-type foci proportional to the concentration of MLV used for superinfection[8]. The response of this line of S+L− cells to superinfection with MLV can be used as the basis for a rapid and sensitive assay technique, the details of which are described in this report.

S+L− cells were obtained by two successive isolations of individual colonies from microplates (Falcon Plastics, Los Angeles) inoculated with the "C-116" line, a mixture of S+L− cells and apparently normal cells[8]. This procedure increased the proportion of S+L− cells in the mixed population to approximately 40% from the 7% in the original C-116 cell line, and a corresponding increase in sensitivity to focus induction was noted.

Table 1 Focus Induction in S+L− Cells by Murine Leukaemia Virus (IC Isolate)

Virus dilution (0.2 ml./dish)	Focus counts	Average No. foci/dish	Titre estimate*
$10^{-3.1}$	Confluent	Confluent	—
$10^{-3.6}$	Confluent	Confluent	—
$10^{-4.1}$	41, 64, 50, 68	55.8	$10^{6.55}$
$10^{-4.6}$	12, 13, 26, 18	17.3	$10^{6.54}$
$10^{-5.1}$	8, 5, 6, 6	6.3	$10^{6.60}$
Control	0, 0, 0, 0	0	—

* Estimate of focus-inducing units/ml. in original MLV preparation based on numbers of foci at each virus dilution.

For leukaemia virus focal assays, S+L− cells were plated in 60 mm plastic Petri dishes at a concentration of 10^5 cells per dish and infected the following day with dilutions of MLV. Five days after infection, foci could be easily seen by microscopy. These foci appeared as lytic areas in the confluent cell sheet characterized by the presence of grape-like clusters of round cells (Fig. 1). Alternatively, infected plates could be stained with May-Grünwald and Giemsa, and the foci counted by microscopy (Fig. 2). The numbers of foci produced by a variety of MLV preparations studied to date were directly proportional to the concentration of virus (Table 1). Friend, Moloney and Rauscher murine leukaemia viruses have all been used to produce foci by this assay technique. Standard preparations of these viruses contained more than 10^6 infectious units per ml. as calculated from the numbers of detectable foci induced in S+L− cells. Radiation leukaemia virus (RadLV)[9] also induced similar cellular changes in S+L− cells, although the foci were distinctly smaller in size and contained few round cells, suggesting that this virus multiplies poorly or not at all in the target cells. Active MSV could be detected in culture fluids from all S+L− assay plates which contained MLV-induced foci.

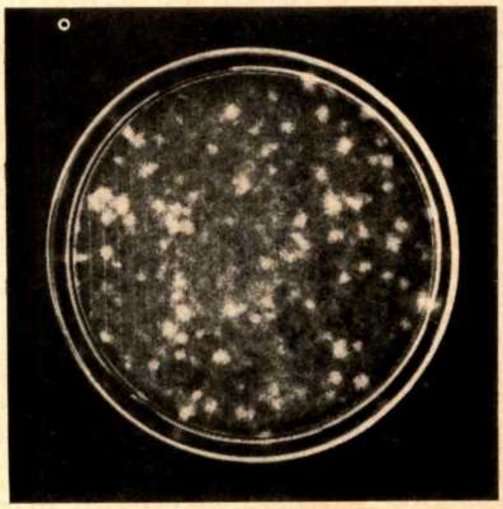

Fig. 2. Petri dish (60 mm) containing approximately 80 foci, 5 days after superinfection of S+L− cells with diluted MLV. May-Grünwald and Giemsa stain; oblique lighting.

Antiserum to the IC isolate of MLV[10], prepared in BALB/c mice by University Laboratories, Highland Park, New Jersey, was highly active in neutralization tests using the S+L− cell assay system. In a two dimensional reaction in which the quantities of both IC virus and its specific antiserum were varied, the proportion of virus neutralized by a given dilution of serum seemed to be independent of the number of focus-inducing units of leukaemia virus (Table 2).

Table 2 Neutralization of Murine Leukaemia Virus (IC Isolate) by Homologous Mouse Antiserum

Antiserum dilution (final)	Focus-inducing units of IC virus added:						
	3,160	1,000	316	100	31.6	10	0
1 : 20	35*	7	2	1	—	—	—
1 : 40	140	29.5	15	2.5	—	—	—
1 : 80	C†	112.5	45	14	—	—	—
1 : 160	C	C	142	33.5	11	—	—
1 : 320	C	C	C	65.5	17.5	—	—
Control	C	C	C	99.5	29.5	10	0

* Average number of foci in two Petri dishes.
† Confluent.

The sensitivity of focus induction in S+L− cells as a measure of MLV activity was compared with that of several other *in vitro* assay techniques. Dilution end point estimates of the amount of replicating virus present in a preparation of IC leukaemia virus were determined in normal 3T3FL[8] mouse cells by measuring induction of interference to MSV or by recovery of "helper" activity for MSV. Quantitatively, these assays gave results which were in close agreement with titres of the same leukaemia virus preparation based on focus assays in S+L− cells. In addition, a preparation of Rauscher leukaemia virus previously assayed in the XC plaque test by Dr Willie Turner of the National Cancer Institute was found to have an identical titre when assayed by focus induction in S+L− cells.

The close correlation between the number of focus-inducing units of MLV in a leukaemia virus preparation and the end point for virus replication measured by several different methods indicates that MLV replication is necessary for focus induction in S+L− cells. Leukaemia viruses such as RadLV, which replicate poorly or not at all in mouse cell cultures, may still be detected by their ability to rescue transforming MSV from S+L− cells, a possibility which is currently under investigation.

Cell lines containing mixtures of S+L− and normal cells develop MLV-induced foci which are easier to enumerate than do lines containing only S+L− cells, since the latter do not readily form confluent monolayers. The quantitative effect of the presence of normal cells together with S+L− cells in the assay system was determined by infecting a mixed cell line with terminal MLV dilutions. Cells from assay plates which did not contain overt foci were passed blindly for 17 days and then tested for MSV production. The MLV titre calculated directly from the numbers of foci induced in the mixed cell line differed only two-fold from the end point dilution estimate of MLV activity based on recovery of MSV from the same cells. These results indicate that focus assays in mixed cell lines detect all, or nearly all, of the MLV capable of replicating in these cells. Passage of two different mixed cell lines for periods of up to 3 months in two different laboratories has not resulted in any noticeable quantitative change in focus formation by MLV, as might be expected if there were a marked change in the proportion of S+L− cells in the population.

In summary, focus induction by MLV in mouse cell lines containing relatively high proportions of S+L− cells is an exceedingly simple and convenient method for the detection and quantitation of murine leukaemia viruses and is comparable in sensitivity to other *in vitro* methods currently in use.

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Participation of θ-Bearing Cell in an *in vitro* Assay of Transplantation Immunity

FOR several humoral immune reactions, cellular interaction between thymus processed and non-thymus processed lymphocytes is required[1-4]. Lymphoid interaction has also been demonstrated in allograft immunity[5], in the graft versus host reaction[6-8] and in an *in vitro* heterograft reaction system[9]. Both in humoral[2-4,10] and in transplantation immunity[9], the cell which initiates the response—the antigen reactive cell—is derived from the thymus. The nature of the effector cell, however, is known only in the case of certain humoral immune reactions, in which it has been demonstrated that antibody is secreted by the non-thymus processed, bone marrow-derived cell[11,12]. The origin of the effector cell in transplantation reactions is unknown.

We have used anti-θ AKR serum[13] to determine whether the effector function (*in vitro* destruction of target cells) of immune AKR lymphocytes is dependent on cells of thymic origin. Such serum has been shown to eliminate selectively thymus derived cells from a heterogeneous lymphoid cell population[14].

Young AKR mice were grafted with C57Bl/6 skin and 11 days later their draining lymph nodes were collected. Suspensions of the sensitized lymphoid cells were prepared and treated with various dilutions of C3H anti-θ AKR serum or normal C3H serum, in the presence or absence of complement. After treatment lymph node cells were plated on C57Bl/6 target fibroblasts prelabelled with ^{51}Cr for the assay of immune lysis[9,15]. Untreated, sensitized and unsensitized AKR lymph node cells were also assayed.

The results of the *in vitro* graft reaction are presented in Table 1. An inhibition of target cell lysis of approximately 20% was observed when sensitized lymph node cells were incubated with normal serum and complement, or with anti-θ serum without complement. This decrease in lytic activity (compared with untreated, sensitized lymph node cells) presumably reflects some damage to the cells caused by

Table 1 Effect of Anti-θ AKR Serum on the Ability of Sensitized AKR Lymphocytes to lyse C57Bl/6 Fibroblasts *in vitro*

Experiment No.	Dose and type of lymphocytes	Treatment	c.p.m.* released	c.p.m.* total	Net %† ^{51}Cr released	% inhibition
1	Spontaneous release ‡		2,482	9,092	—	—
	5 × 10^6 sensitized cells	None	3,498	9,058	15.4 ± 2.2	0.0
		0.05 ml. a-θ	3,251	8,778	12.2 ± 0.2	20.8
		0.05 ml. a-θ + C′	2,583	9,445	1.4 ± 0.7	90.9
		0.10 ml. a-θ + C′	2,560	9,523	1.3 ± 0.6	91.6
2	5 × 10^6 sensitized cells	None	3,670	9,402	17.2 ± 1.3	0.0
		0.05 ml. normal serum + C′	3,426	9,579	13.3 ± 0.8	22.6
		0.05 ml. a-θ + C′	2,615	8,940	1.9 ± 0.9	89.0
		0.10 ml. a-θ + C′	2,549	9,037	1.0 ± 0.5	94.2
3	Spontaneous release ‡		2,607	9,079	—	—
	10 × 10^6 non-sensitized	None	2,774	8,736	2.7 ± 2.5	—
	10 × 10^6 sensitized cells	None	3,760	7,536	23.3 ± 1.9	0.0
		0.05 ml. normal serum + C′	3,227	7,250	17.0 ± 0.9	27.0
		0.005 ml. a-θ + C′	3,534	7,838	17.7 ± 1.4	24.0
		0.01 ml. a-θ + C′	3,850	8,755	20.2 ± 1.1	13.4
		0.02 ml. a-θ + C′	3,223	7,878	11.3 ± 4.7	51.5
		0.05 ml. a-θ + C′	2,501	8,492	0.8 ± 2.0	96.6
		0.10 ml. a-θ + C′	2,329	8,139	0.0	100.0

Female AKR/J mice, 2.5 months old, were grafted with C57Bl/6 skin. Eleven days later the draining lymph nodes were collected and a cell suspension prepared in Eagle's medium plus horse serum (20%). Lymphoid cells were preincubated with varying amounts of anti-θ serum or normal C3H serum, in the presence or absence of Difco guinea-pig complement (C′). After 1 h lymphoid cells were washed and 5 or 10 × 10^6 cells were plated on fibroblast monolayers labelled with ^{51}Cr (0.7 – 1.0 × 10^6 fibroblast/plate). ^{51}Cr released was determined after 48 h[9,15].

* Mean value of two to seven replicates.

† Net % ^{51}Cr released was calculated according to Brunner *et al.*[16].

‡ Target monolayers labelled with ^{51}Cr were incubated for 48 h with Eagle's medium and horse serum only, to determine spontaneous release of ^{51}Cr.

the additional handling (centrifugation, incubation, washing and so on). On the other hand, sensitized cells pretreated with 0.05–0.10 ml. of anti-θ serum per culture plus complement lost essentially all their lytic activity and this effect is antibody-dose dependent (experiment 3, Table 1). Unsensitized AKR lymphocytes did not produce any lytic effect, indicating that it is unlikely that during the assay period any additional sensitization occurred.

We (unpublished observations) and Raff[14] have observed that anti-θ immune serum eliminates 85–90% of thymus lymphocytes, but only 50% of lymph node and 30% of spleen lymphocytes. In cultures containing the highest concentration of anti-θ serum, and in which lytic activity was essentially completely abolished, a considerable number of lymphoid cells were still viable at the end of the assay period. These might be cells which do not bear the θ antigen marker.

Our results suggest that the *in vitro* lytic activity of sensitized lymph node cells depends on the function of cells bearing the θ antigen. These findings exclude the possibility that the lytic function is performed solely by bone marrow-derived or other cells not bearing the θ marker, but they do not demonstrate in an exclusive way that the thymus-derived cell is the only cell causing the cytolytic effect. The fact that we have only a thymus-specific reagent (anti-θ), and that at present we do not have lymphotoxic immune sera of other specificities, leaves open another possible interpretation, besides an exclusive effector role of thymus derived cells. The cytolytic damage could be caused by cells of more than one type—thymus and some other cell type, such as bone marrow-derived—wherein one cell would be involved in causing the actual target cell destruction and the other would fulfil some auxiliary function.

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Induction of Lactogenesis and Abortion by Prostaglandin F$_{2\alpha}$ in Pregnant Rats

THE withdrawal of ovarian progesterone at the end of pregnancy seems to be the essential step in the initiation of lactation in pregnant rats[1-5]. Although there is a decrease of plasma progesterone concentration before parturition[6,7], the mechanisms involved in the regression of the corpus luteum at parturition are unknown. It is known[8-10] that the uterus is concerned with the regression of the corpus luteum in the rat and the uterine luteolytic seems to involve a substance transported in the blood[10]. The discovery of prostaglandins in menstrual fluid and human endometrium[11,12] and the luteolytic action of prostaglandin F$_2$ (PGF$_{2\alpha}$) demonstrated in pseudopregnant rats[13] and normal guinea-pig[14] indicate a possible participation of prostaglandin at the end of pregnancy. The high concentration of PGF$_{2\alpha}$ in the amniotic fluid during labour[15] gives support to this hypothesis.

I have investigated the effect of PGF$_{2\alpha}$ in eight pregnant rats of the Instituto strain, housed in individual cages. They were injected intraperitoneally with 1.2 mg of PGF$_{2\alpha}$ in four doses of 0.3 mg each, every 4 h on day 17 (two rats) and day 18 (six rats) of pregnancy. PGF$_{2\alpha}$ was prepared as recommended by the makers (Upjohn). A control group of ten rats was injected with four doses of normal saline on day 17 of pregnancy. The following day, 12 and 17 h after the administration of the last dose of saline or prostaglandin, an oxytocin test[4] was performed to determine the onset of lactogenesis.

All animals were checked several times a day for signs of abortion. After parturition, maternal behaviour was watched in each treated rat.

None of the control rats gave a positive response to the oxytocin test. In this strain lactogenesis takes place 12 h before parturition on day 22 (ref. 4). All control rats delivered normal foetuses at term. But when the oxytocin test was applied to the eight treated rats 15 h after the last injection of PGF$_{2\alpha}$ visible milk appeared. No rats gave a positive response in the first test. It is interesting that after the last dose of PGF$_{2\alpha}$, rats adopted the typical posture of parturition for at least 1 h; contractions were also observed through the abdominal wall. Four rats were injected with 100 mU of oxytocin 30 min after the last dose of prostaglandin, to see whether abortion could be induced. None aborted, but blood was seen in the vagina of some rats. On day 20 of pregnancy all rats treated with PGF$_{2\alpha}$ delivered small foetuses, some of them alive. Maternal behaviour was studied by giving a foster litter to each rat on the day after parturition. Seven rats showed normal maternal behaviour but only two were able to feed the young.

These results show clearly that PGF$_{2\alpha}$ can induce lactogenesis and advance parturition when injected into pregnant rats. According to previous knowledge[13,14] PGF$_{2\alpha}$ may have a luteolytic effect in pregnant rats and may be responsible for the decrease in progesterone at the end of pregnancy. There is no evidence about the mode of action of PGF$_{2\alpha}$ in pregnant rats. The suggestion of a venoconstrictor action affecting the life span of the corpus luteum[13] has been shown to be incompatible with the normal development of the rest of the ovary after treatment with prostaglandin[14]. Further work is needed to clarify the function of PGF$_{2\alpha}$ as the luteolytic factor before parturition.

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Production of Lytic Plaques of Viral Origin in *Penicillium*

THE presence of virus particles in fungi is now established on the basis of observations in *Agaricus* (*Psalliota*) *bisporus* and in *Penicillium stoloniferum*[2,3] and *P. chrysogenum*[4]. Viruses in *A. bisporus* cause several malformations of the fruiting body[5] and some morphological variations of the colony in *P. stoloniferum*[3]. Small patches of white aerial mycelium have frequently been observed on the surface of fungi and we have confirmed this for *P. citrinum* and *P. variabile* grown on potato glucose agar at 24° C. When these organisms are grown on 18% lactose, 1% peptone, 2% agar, distilled water (*p*H 6·5) (medium A) at 24° C, lytic plaques are observed on the reverse of the patches of white aerial mycelium (Fig. 1*a*, *b*), which are morphologically similar to those produced by bacteriophages in bacteria and in streptomycetes. The mycelium taken from the centre of the lytic area consists of swollen hyphae, wholly lysed or with very little cytoplasm. Observation with the electron microscope, after fixation with phosphotungstate (PTA) at *p*H 7, has shown that the hyphae yield a large amount of virus particles (2 to 100 per field) as previously observed[1-4]. The particles have a hexagonal shape, with no tail and a diameter of 400–500 Å.

We tried to determine whether the presence of virus could cause some modification of the normal morphology of the two species under examination. Two culture types were isolated in medium A; type 1 was obtained from the mycelium taken from the centre of a lytic plaque; type 2 was obtained from mycelium taken from the white patches present on the colony surface. Type 1 gave moist, yeast-like colonies without aerial mycelium, and which were sterile; type 2 gave fluffy round colonies, with abundant aerial mycelium; they also were sterile. Only the type 2 colonies contained a large amount of virus particles (15–30 per field) like those observed in the lytic plaques. The virus particles were not found in the type 1 colonies, nor in the normal mycelium of the two species of *Penicillium* under examination. Type 2 colonies, grown at 30°–32° C, reverted to normal—that is conidia were formed again. At these temperatures therefore it seemed that the fungus recovered from the virus infection, as observed by others[1,3] for subcultures at 24° C.

To reproduce the lytic plaques, we broke each plaque with a cotton swab, took out the infected mycelium and the conidia of the surrounding healthy mycelium, and smeared this evenly on 20 ml. of medium A in 10 cm Petri dishes (the thickness of the agar seemed to be critical). After 5–10 days at 24° C a

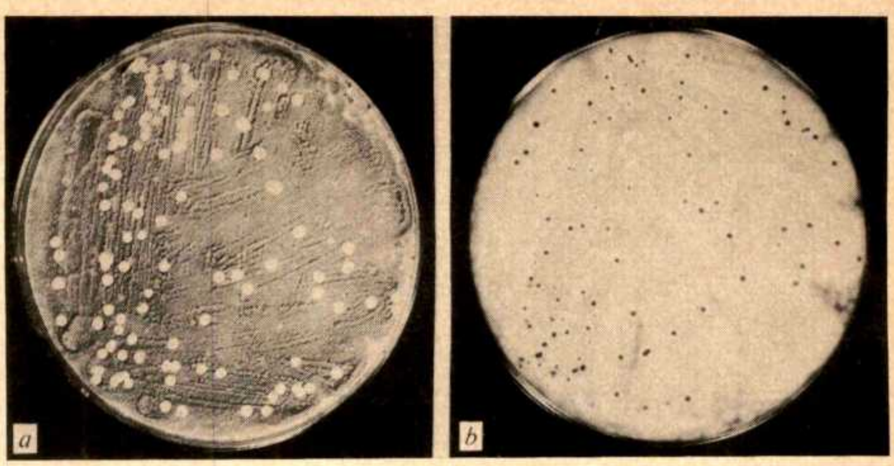

Fig. 1 *a*, *P. variabile*, upper surface of the colony with several patches of white aerial mycelium. *b*, Reverse side of the colony of *P. variabile* showing the presence of several lytic plaques which coincide with the white patches.

large number of lytic plaques of various shapes and sizes were observed, this being related to the type of carbon source and to its concentration. Using medium A, it was found that the optimal carbon source was given by 10% sucrose or 18% lactose. The lytic plaques are inhibited by the addition to medium A of the sodium salt of mycophenolic acid at the minimal concentration of 1 μg/ml. Attempts to transmit the infection from infected to healthy strains have proved unsuccessful.

It is possible to draw the following conclusions. Two species of *Penicillium* show lytic plaques containing some viruses, similar to those produced by bacteriophages. Patches of white aerial mycelium seen at the surface of the colonies of the two species of *Penicillium* result from a viral infection that in turn brings about a marked morphological modification of the fungus. The yeast-like colonies (type 1) do not show any virus particles. Their stability, even when grown at 30°–32° C, suggests that in them the virus is linked to the chromosomes, that is, it is in temperate form. Mycophenolic acid inhibits the appearance of lytic plaques and therefore it seems to have an antiviral activity in fungi similar to that shown against some animal viruses[6,7].

This similarity of activity suggests the possibility of using the fungi as quick tests for the evaluation of new antiviral compounds following the same procedure used in the evaluation of the antibacterial activity of the antibiotics.

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Control of Glycolipid Synthesis in a Cultured Hamster Cell Line

THE synthesis of complex ceramide glycolipids can be depressed in virus-transformed animal cell lines. The initial observation was made when Hakamori and Murakami[1] showed that polyoma virus-transformed BHK21 cells contain less haematoside than untransformed cells. Mora *et al.*[2] found in subconfluent cultures of mouse cell lines that concentrations of haematoside were comparable in spontaneously transformed and untransformed lines but that SV40 virus transformation led to a decrease in the concentrations of other gangliosides. We have found that transformation of NIL2 hamster cells leads to a depression in the synthesis of three glycolipids. The synthesis of these same three specific components may, however, be sub-optimal in normal NIL2 cells kept in an actively growing non-contact inhibited state.

NIL2 cells[3] were grown by standard methods in Eagle's medium with 10% foetal calf serum. Lipids were labelled by growing cells for 2 days in the presence of 1-^{14}C-palmitate (1.3 μCi/ml., 55 μCi/μmol). Cell sheets were washed with phosphate-buffered saline and stored at −20° C before analysis. Cells were removed by scraping and plates were washed with methanol. After drying, the cell residue was extracted with chloroform–methanol (2 : 1) and chromatographed on thin-layer silica gel plates by the method of Gray[4]. An autoradiograph of a typical chromatogram is shown in Fig. 1.

To test the effect of cell density on glycolipid synthesis, cells were plated at high (5×10^4 cm^{-2}) and low (5×10^3 cm^{-2}) density on segments in the same 9 cm Petri dish separated initially by a ridge of melted plastic. After incubation overnight to allow attachment, the medium was made confluent and labelled palmitate was added. After 2 days of labelling and growth at 37° C, cells from the two areas of the plate were counted and extracted separately. Comparisons were made with extracts from equal numbers of cells. After chromatography and autoradiography the radioactive areas were removed from the thin-layer plates and counted. The results of such an experiment are shown in Table 1. Although approximately equal labelling occurred in the principal phospholipids and also in haematoside (GM$_3$) and ceramide dihexoside (CDH) it is clear that in cells growing at the lower cell density there is much less incorporation into ceramide trihexoside, galactosylgalactosylglucosyl ceramide (CTH), the aminoglycolipid, β-N-acetylgalactosaminylgalactosylgalactosylglucosyl ceramide (AGL) and the unidentified ceramide (CX).

Similar incorporation experiments were carried out with NIL2 cells transformed by hamster sarcoma virus[5] and an adeno 7/SV40 hybrid virus. In both cases it was found that there was normal synthesis of phospholipids and of haematoside and ceramide dihexoside. Little or no CTH, AGL or CX could be found, however, in these transformed lines. It is interesting that the same three glycolipids, and only these

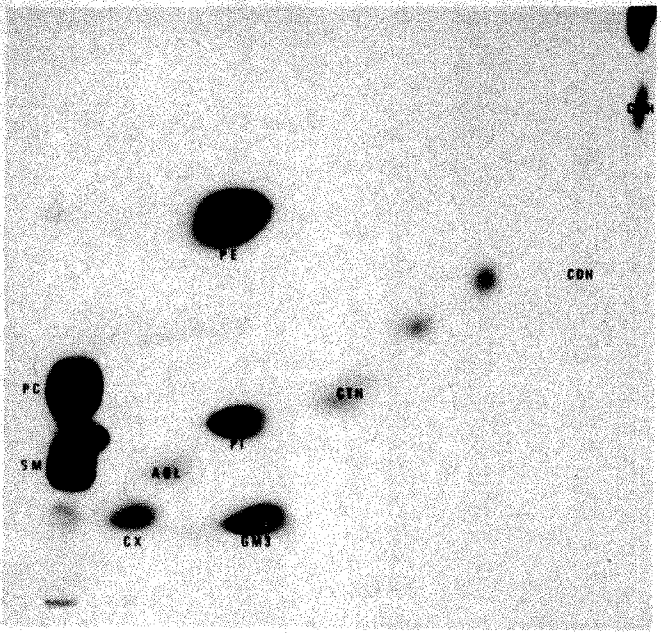

Fig. 1 Autoradiograph of a thin-layer chromatogram of NIL2 cells labelled with 1-^{14}C-palmitate. The origin is at the lower left. Fatty acids and neutral glycerides run at the upper right corner. SM, Sphingomyelin; PC, phosphatidyl choline; PE, phosphatidyl ethanolamine; PI, phosphatidyl inositol; CX, an unknown ceramide that generates ceramide dihexoside on partial acid hydrolysis; GM$_3$, haematoside; AGL, ceramide tetrahexoside; CTH, ceramide trihexoside; CDH, ceramide dihexoside; and CMH, ceramide monohexoside.

three, are synthesized more actively by contact inhibited cells than by sparse untransformed NIL2 cells. The result suggests that the lack of these complex glycolipids in transformed NIL2 cells could simply be a reflexion of the lack of normal contact inhibition and lack of growth restraint in transformed cells. A full report will be published elsewhere[6].

Table 1 Incorporation of 1-^{14}C-Palmitate into Glycolipids and Phospholipids of NIL2 Cells

Lipid*	Incorporation (c.p.m. × 10^{-3}) Low cell density area	 High cell density area
PC+SM	928	1,071
PE	187	165
CX	3.5	13.6
GM$_3$	23.6	34.7
AGL	1.0	10.6
CTH	2.6	9.5
CDH	0.7	0.8

Cells were labelled for 2 days with high and low density areas on the same 9 cm Petri dish as described in the text. After extraction, chromatography and autoradiography, the autoradiograph pattern was used as a template for removing spots for scintillation counting.

* See Fig. 1 legend for abbreviations.

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Segregation of Univalents on Mini Spindles

MANY authors have reported that the behaviour of univalent chromosomes at meiosis is irregular. At metaphase they tend to lie off the metaphase plate and closer to the poles than the bivalents; and it has been suggested that this is because the univalents move to the poles earlier. In the triploid species *Leucopogon juniperinus* univalents are close to the poles at metaphase, but serial sections show that they are not in the same plane as the spindle on which the bivalents are positioned (Fig. 1). Closer examination of the metaphase cells shows that the univalents are attached to a separate, much reduced spindle, which is attached to the same pole as the "bivalent" spindle but is formed in a different plane (Fig. 1, cells 2 and 3).

This observation suggests that the difference in behaviour of the chromosomes is associated with their lack of pairing. If in a plant which normally has one accessory chromosome (univalent at meiosis), this chromosome becomes doubled, then the two homologous chromosomes can pair in meiosis and behave on the metaphase plate as a normal bivalent[1]. Similar behaviour has been reported for the unpaired *X* chromosome in the mantid *Humbertiella indica*, in which the univalent *X* was attached to only one pole of the meiotic spindle. In abnormal cells in which the *X* had precociously divided, sex bivalents were formed which behaved normally on the spindle[2]. So this unusual behaviour of univalents at meiosis results not

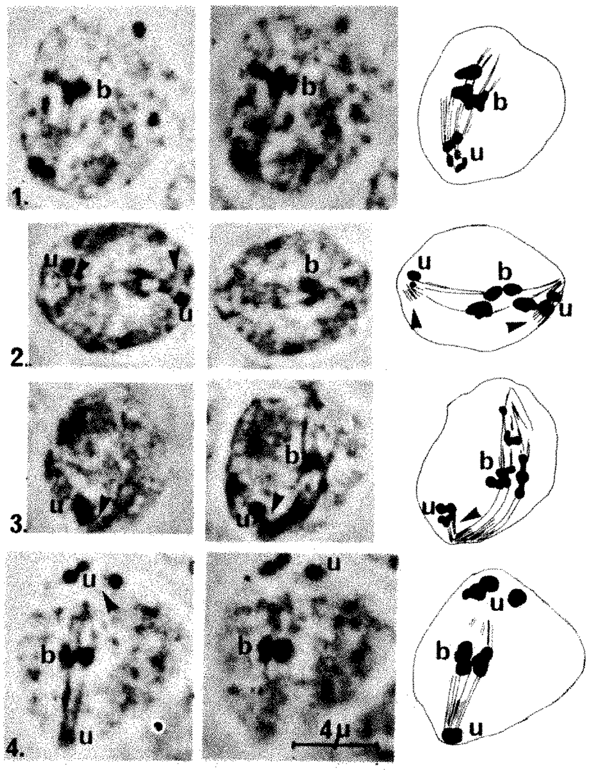

Fig. 1 Chromosomes of *L. juniperinus* during metaphase.

from the properties of individual chromosomes but from their unpaired state.

In most plant species the behaviour of univalents is non-random in the embryo sac mother cell and random in pollen mother cells[3,4]; in *Leucopogon juniperinus*, however, it is non-random in both[5]. During microsporogenesis, at anaphase 1, all four univalents go to one pole with a frequency of 55.7% compared with a random expectation of 12.5%. Because there is a cytoplasmic gradient in embryo sac mother cells and it has been deduced that there is a gradient in the pollen mother cells of *Leucopogon*, it is very likely that non-random behaviour of univalents is in response to a cytoplasmic gradient.

The univalents in *L. juniperinus* are arranged on their small spindles at the poles when the bivalents move on the metaphase plate, so that their response to the cytoplasmic gradient must occur before metaphase. The response to the cytoplasmic gradient determines not only the unequal segregation of univalent chromosomes but also whether the small spindles will be set up at one or other or both poles.

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DDE reduces Medullary Bone Formation in Birds

DURING the past two decades residues of certain chlorinated hydrocarbons, especially DDT, have caused declines in the populations of various carnivorous birds in the North Temperate Zone by reducing their reproductive success[1-3]. Contaminated birds lay eggs with abnormally thin, insufficiently calcified shells, so that there is increased egg breakage and embryonic death[4-9]. Although adult mortality, abnormal behaviour, delayed ovulation and nesting, egg eating, and failure to lay eggs also sometimes result from such contamination[1-3,8-11], the thin eggshell phenomenon is the chief cause of the declines in population[3,6,8].

Chlorinated hydrocarbons induce hepatic microsomal enzymes that hydroxylate steroids[12,13], including oestrogens, which are produced in increased amounts by the avian ovary before egg laying. In birds of both sexes, oestrogens mediate deposition of calcium in the medullaries, or hollow parts of the skeleton[14], where it serves as a labile calcium source for eggshell formation. Chlorinated hydrocarbons should therefore reduce medullary bone formation as well as eggshell calcification. We have investigated this possibility by injecting an oestrogen into male pigeons and determining whether the ingestion of chlorinated hydrocarbons by some of these birds reduces medullary bone formation. *p,p'*-DDE[1,1-dichloro-2,2-*bis*(*p*-chlorophenyl)ethylene] was used because it is the most widespread chlorinated hydrocarbon pollutant, and it has a substantial effect on eggshell thickness.

Seven groups, each of four 5 yr old male silver king pigeons, were injected twice weekly with doses of β-oestradiol ranging from 0.05 to 0.70 mg per day during the spring of 1969. At each dose, two birds received feed containing 100 p.p.m. of DDE dissolved in corn oil, and two control birds received feed with an equal amount of corn oil. At the end of 4 weeks, all birds were decapitated, and both femurs were removed, calcined at 675° for 8 h, and weighed. The average combined weight of both femurs of ten other 5 yr old male pigeons of comparable weights given neither oestradiol nor DDE was 0.793 g. This value was subtracted from all femur weights of experimental birds to give the medullary bone weights (Table 1).

Table 1 Femur Medullary Bone Weights

β-Oestradiol (mg/day)	Control birds (g)		DDE birds (g)	
0.05	0.284	0.393	0.213	0.139
0.10	0.201	−0.060	0.219	0.037
0.20	0.201	0.164	0.165	0.123
0.30	0.227	0.409	0.120	0.110
0.40	0.324	0.293	0.037	0.109
0.50	0.405	0.315	0.125	0.275
0.70	0.444	0.355	0.264	0.126
Overall mean weights	0.283 g		0.147 g	
Expressed in %	100%		52.1%	

Medullary bone formation as a function of the dose of oestradiol was inconclusive, but when the data were pooled for the two groups, medullary bone formation by the birds fed DDE was only 52.1% as much by weight as that in control birds. The difference between the two groups was significant at the 0.01 level according to the Mann–Whitney U test[15]. This finding is consistent with the reduced level of circulating oestradiol found by Peakall and believed to result from induced hepatic hydroxylation[9]. Enzyme induction would also explain the altered behaviour, failure to lay, and late ovulation and nesting occurring among the carnivorous birds[3,9]. Peakall and Bitman have presented convincing evidence, however, that the thin-shelled eggs are caused primarily by inhibition of carbonic anhydrase, an enzyme required for shell formation in the shell-forming region of the oviduct[3,7,9]. The diminished reproductive success of these birds is therefore explainable by the simultaneous occurrence of enzyme induction in the liver and enzyme inhibition in the oviduct, both resulting from these chlorinated hydrocarbon pollutants.

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Method for Measuring the Leaf Surface Area of Complex Shoots

A KNOWLEDGE of leaf surface area is essential for many plant physiological and ecological studies[1-5]. Conventional measurements based on leaf dimensions are invariably laborious and often only approximate. Other methods aimed at increasing the speed and accuracy of the measurements, such as photoelectric techniques[6,7], are only really applicable to broad leaved species. For microphyllous and needle leaved species the only reliable method so far has been to calculate the surface areas of selected leaf samples from measurements of length and circumference, then to extrapolate the values to whole shoots on the basis of leaf numbers or fresh weights[5,8]. Doronichev[9] has attempted to simplify the measurements for conifer shoots by determining the adsorption of methylene blue from aqueous solutions on the assumption that a monomolecular layer is formed on the surface and that each mg methylene blue adsorbed corresponds to a surface area of 1.05 m^2. For most plant shoots, however, the change in methylene blue concentration is far too small to be accurately measured using standard photo-densitometers.

We have developed a method on somewhat similar principles that is much more applicable for general use. A shoot is removed and thinly coated with the pressure sensitive adhesive, 'Adsol 400' (Adhesive Solutions Ltd, Rickmansworth), by dipping it two or three times into a solution diluted 1 : 7 by weight with benzene. After about 5 min, to allow the benzene to evaporate, the shoot is weighed and then covered with small Ballotini glass balls (Jencons (Scientific) Ltd, Hemel Hempstead) by pouring the balls over the shoot whilst it is slowly rotated. The shoot is then vigorously tapped or shaken to remove loose balls and reweighed. The balls form a uniform layer over the whole of the exposed surface (Fig. 1), so the gain in weight is directly proportional to the area covered. Leaf and stem surface areas can be separated by removing the needles and repeating the exercise on the stem only, after washing off the balls and adhesive with benzene.

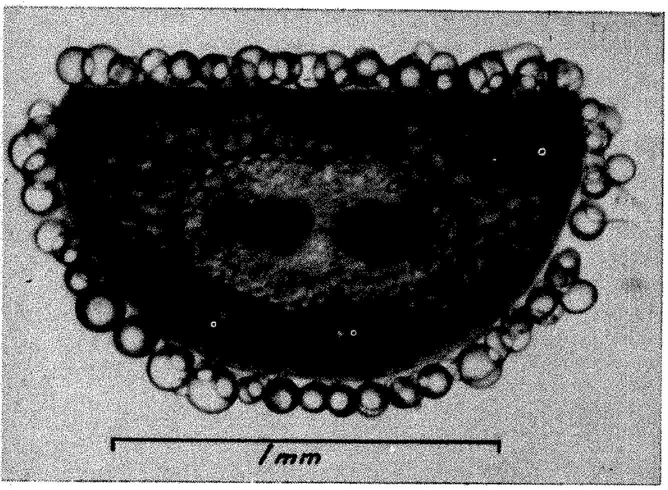

Fig. 1 T. S. Corsican pine needle coated with Ballotini glass balls.

Tests on a range of artificial flat and cylindrical surfaces showed that balls of approximately 0.11 mm diameter gave the best compromise between a large weight increase per unit surface area and a more consistent packing distribution. For this size of glass ball, the gain in weight was 13.6 ± 0.1 mg cm^{-2}.

For several Norway spruce shoots (single needles), leaf surface areas determined by the glass ball method and ranging from 17 to 30 cm^2 agreed to within 3% (s.e. ± 1.4%) with those calculated from the dimensions of a 15% random sample of needles. For each shoot, the glass ball method took 10–15 min, the conventional method several hours. In the case of mature or near mature Scots pine shoots, the situation is rather more complicated because most of the paired needles are separated at various distances from the base so that the exposed needle surface area as measured by the glass balls is less than the total surface area. When allowance was made for this in the direct measurements, the two methods again agreed to within 3% (s.e. ± 0.1%) for areas of 26 to 34 cm^2. In many physiological studies, for example, those concerned with gaseous exchange or evaporation, a knowledge of the exposed area of leaf surface is probably more relevant than that of the total surface area. The method can be readily adapted, however, to give total leaf surface areas, for example, by removing one of the needles from each pair so that half the total leaf surface area can be determined.

This new method is simple, rapid and, as far as we can judge, accurate; because it is non-destructive, measurements can be replicated on the same shoot. It can also be used for other complex structures, provided that these are sufficiently rigid to prevent adhesion between surfaces when the adhesive is applied. Different Ballotini ball grades can be chosen according to the detail of the surfaces studied and the precision required. It is important in practice to use dilute solutions to avoid loss of surface detail through the accumulation of the adhesive; with the ridged stems of Scots pine, for example, covering with adhesive decreased the circumference by about 4%. Because of the need to ensure a complete and uniform coating of all surfaces with the balls, a fluidized air bed method may prove more effective than the simple pouring system used here; but our experience has been that the latter method is satisfactory for most purposes.

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Bats and Fog

ON windless evenings fog commonly forms in dense, sharply defined patches, especially in sheltered bays of ponds. As the evening progresses and the temperature falls, these patches may grow and coalesce, advancing over the pond but maintaining a sharp front at which visibility changes profoundly within a few metres. In such conditions insectivorous bats hunting over the water have been observed to turn back at the fog front as if at a solid wall, even though their hunting area may become severely restricted. This behaviour suggests that fog may have a direct effect on echo location.

Meteorological studies[1,2] have shown that stable fog consists of water drops with diameters ranging from about 1 μm to about 100 μm. The range of size varies in different fogs but is always rather wide because of coalescence. Drops smaller than 1 μm form a "blue haze" due to selective Tyndall scattering of shorter light wavelengths; drops from 100 to 400 μm fall steadily as "drizzle" while drops from 400 to 1,000 μm form "rain", although much larger drops may be formed in thundery showers.

In 1896 Rayleigh[3], discussing the influence of fog on the transmission of audible sounds, wrote, "In spite of isolated assertions to the contrary, it was generally believed . . . that the influence of fog was prejudicial. Tyndall's observations prove satisfactorily that this opinion is erroneous, and that the passage of sound is favoured by the homogeneous condition of the atmosphere which is the usual concomitant of foggy weather". Furthermore, " . . . the disturbance of plane sonorous waves by a small obstacle . . . depends upon the ratio of the diameter of the obstacle to the wavelength of the sound". The wavelengths of the ultrasonic spectrum of bats range from a little more than 2 mm to about 20 mm, as shown by the double ordinate scale of Fig. 1 (upper). Even the largest fog drops thus have a diameter which is only 1/20 of the shortest wavelengths used by bats and 1/70 of the wavelength at 50 kHz. The presence of fog should therefore produce little disturbance by scattering to the propagation of bat sounds.

Rayleigh also showed, however, that liquid drops resonate mechanically at frequencies dependent on their dimensions. His formula simplifies for spherical water drops in air to approximately

$$f = \left(\frac{500}{d}\right)^{1.5}$$

where f is the resonant frequency in kHz and d is drop diameter in μm. This relation is shown in Fig. 1 together with ranges of drop size for three natural fogs, plotted from data given by Houghton and Radford[1]. It is convenient to consider the frequency band used by bats as 15–150 kHz in general, corresponding to droplet sizes from 82 μm to 18 μm. The range of frequencies for British species is covered by droplet sizes from 70 μm (about 20 kHz) to 22 μm (110 kHz).

Fog containing droplets in this range will theoretically have a strong influence on the propagation of echo location signals from a bat. Each droplet will absorb sound energy at its resonant frequency and will subsequently reradiate it over a relatively long time. Thus there will be no immediate and sharp echo return but a slowly decaying "ringing", as from a struck bell. Although each droplet will be sharply tuned because of its almost perfect spherical shape, the effect of any given fog will be spread over a frequency range that depends on the spectrum of droplet sizes present. The fog will thus be opaque to ultrasound as to light, but with one major difference. The droplets are large compared with light wavelengths so that all colours are scattered and fog appears white in, say, car headlamps; but to an ultrasonic echo location system it must be a "black void" with perhaps a faint persistent afterglow. Not only would insect detection become difficult or impossible but there would be a danger of colliding with obstacles or with the ground or water below.

To demonstrate these effects, some simple physical experiments have been performed in the laboratory. Artificial, dense, white fog may easily be produced by dropping small lumps of solid carbon dioxide (cardice) into warm water. The fog is cold and rapidly fills its container until it pours over the edges and rolls across the bench. An ultrasonic loudspeaker was placed in such a vessel facing a calibrated microphone 13 cm away, and short pulses of pure tones were transmitted between the two. The intensity of the signal received in clear air was then compared with that received through thick fog at a number of different frequencies. The amount of attenuation produced by the fog was high and increased with frequency from about 40 dB/m at 20 kHz to 130 dB/m at 80 kHz and to about 190 dB/m (difficult to measure accurately even over 13 cm) at 100 kHz. This means that two of the loudest bats would be inaudible to each other at distances over which detection of faint insect echoes is possible in clear air. Admittedly this was a very dense fog with a "visibility" of only a few centimetres and natural fogs would be unlikely to give such startling values. On the other hand, the spectrum of drop sizes of the artificial fog probably has a peak at a smaller drop diameter than the natural fogs of Fig. 1, for maximum attenuation apparently occurred above 100 kHz.

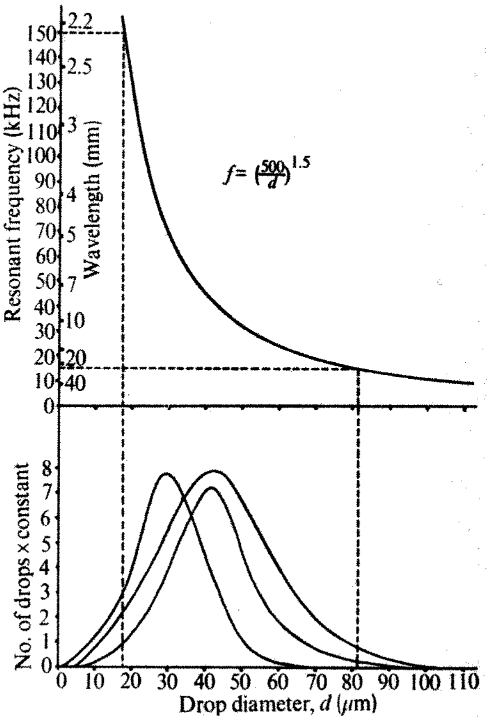

Fig. 1 Above, the resonant frequencies of spherical water drops in air, calculated by a formula derived from Rayleigh[3]. Below, spectrum of drop sizes for three fogs, replotted from volume distribution curves given by Houghton and Radford[1]. The vertical dotted lines delimit the drop sizes resonant between 15 kHz and 150 kHz.

In another arrangement the loudspeaker and microphone were aimed downwards, well above the container, so that transmitted pulses were received after reflexion from the water surface. The pulse generator triggered the time-base of an oscilloscope which then displayed the strong specular echo after the correct propagation delay. When a little cardice was added, the container filled with fog to the brim and the echoes were attenuated accordingly. But no earlier echo could be detected from the smooth surface of the fog. The beamed sound was simply absorbed. Subsequent reradiation of this sound by the droplets could not be detected, suggesting that the droplets are very sharply tuned. The ears of bats are much more sensitive than microphones and might be able to detect this ringing which would form a further source of confusion.

The ecological implications of all this are clear. Insectivorous bats are in any case unlikely to profit by flying in generally foggy conditions because of the paucity of food. Discrete fog patches may develop when hunting is good but it would be dangerous as well as unprofitable for a bat to enter such a bank even if its prey flies into one.

The influence of rain is also worth considering. Bats may be seen hunting in drizzle, though often in a tentative, halfhearted manner. Steady drizzle deters insect flight but there would seem to be no serious hazard to echo location. Sound scattering will still be slight and even the finest drizzle droplets will resonate below 10 kHz. In the sudden, heavy rain of thunderstorms there may be large numbers of insects in the air and bats are often seen to continue active and apparently successful hunting, with rapid turns accompanied by ultrasonic "interception buzzes". Drops of 1,000 μm diameter resonate at 350 Hz but scattering may be appreciable, especially at the highest, "blue" frequencies. The problem is then one of distinguishing insect echoes from the "clutter" of echoes returned by raindrops. The critical difference may be that the drops all fall downwards and maintain a constant reflectivity, whereas flying insects do neither. The work of Webster[4] suggests that the processing of echo signals by bats is sufficiently sophisticated to deal with this situation and this is certainly supported by field observation.

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*p*H of Very Acid Soils

THE purpose of this note is to call attention to the fact that usual methods of measuring soil *p*H[1] seriously underestimate the *p*H of very acid soils, such as those of coal mine spoils[2], cat clays[3] and solfataras[4], in which acidity is due to the presence of free sulphuric acid. Standard methods for measuring soil *p*H involve making a slurry of soil with (usually) distilled water at a 1 : 2, 1 : 5, or 1 : 10 dilution, and reading the *p*H of this slurry. Implicit in this procedure is the assumption that the soil is buffered and hence that *p*H does not change with dilution. This assumption is erroneous in the case of the sulphuric acid soils.

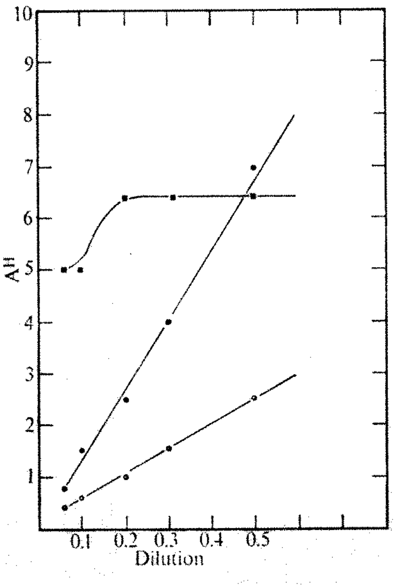

Fig. 1 The dilution curves of three soils. ■, Clay soil, pH$=5.3$; ●, solfatara soil, pH$=1.90$; ○, mine waste soil, pH$=1.30$.

In our work on the microbiology of very acid soils[5] we wanted to know the *p*H values to which the microorganisms were actually subjected; that is, the *p*H of the soil water. To measure this, a slurry of equal parts of soil and water was made and from this slurry a series of dilutions in water were made. The *p*H of each dilution was measured using a Corning combination glass electrode, and a graph was prepared relating hydrogen ion concentration to dilution (Fig. 1). In the case of the sulphuric acid soils, a straight line was generally obtained and this line was then extrapolated back to zero dilution and the hydrogen ion concentration of the soil obtained. If the *p*H of the soil water was desired, the moisture content of the soil was determined and the dilutions then corrected to represent dilutions of the soil. (For example, if the moisture content of the soil were 10% then the initial dilution would be 1 : 20 rather than 1 : 2.) As also shown in Fig. 1, an acidic agricultural soil, being buffered, does not change *p*H significantly with dilution, and hence its *p*H can readily be estimated by the standard procedure.

Table 1 *p*H of Coal Mine Refuse from Pike County, Indiana

Diluent	Method 1 : 2 dilution	 1 : 10 dilution	Estimated *p*H at zero dilution Soil	 Soil water
Distilled water	3.8	4.5	3.5	3.4
1 M KCl	2.3	2.9	—	—
0.01 M $CaCl_2$	2.7	3.2	—	—

Our new procedure was compared with standard procedures for several coal mine spoil and solfatara soils. The results with one representative soil are shown in Table 1. It can be seen that the *p*H value as measured is lower than estimated by standard dilution in distilled water. The *p*H obtained by standard dilution in KCl or $CaCl_2$ is lower than that obtained by our method, but reflects exchange of hydrogen ions by diluent cations[1] and hence does not necessarily represent the *p*H of the soil water. When considering the introduction of plants on coal mine spoils, cat clays, or other very acidic soils, a knowledge of the exact *p*H value, as determined by our new method, should be of significant value.

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BOOK REVIEWS

Second Time Around

Nature and Man: Essays Scientific and Philosophical. By William B. Carpenter. Pp. vi + 483. (Gregg International: Farnborough, Hants, 1970. First published 1888.) $20.20; £8.40.

Social Statics: or the Conditions Essential to Human Happiness Specified, and the First of Them Developed. By Herbert Spencer. Pp. viii + 476. (Gregg International: Farnborough, Hants, 1970. First published 1851.) $18.75; £7.80.

The Wonderful Century: Its Successes and Its Failures. By Alfred Russel Wallace. Pp. xii + 400 + 12 diagrams. (Gregg International: Farnborough, Hants, 1970. First published 1898.) $12.95; £5.40.

The Biographical History of Philosophy from Its Origin in Greece Down to the Present Day. By George Henry Lewes. Pp. xxxvi + 675. (Gregg International: Farnborough, Hants, 1970. First published 1857.) $24.50; £10.20.

The Constitution of Man Considered in Relation to External Objects. By George Combe. Eighth edition, revised, corrected and enlarged. Pp. xx + 507. (Gregg International: Farnborough, Hants, 1970. First published 1847.)

LIKE many British historians, I greeted the first announcement of Gregg International's reprint series of nineteenth century classics with some enthusiasm. One of the most attractive features of this new venture is the emphasis on works illustrating the period's concern with the social and philosophical implications of pre- and post-Darwinian biology.

The need for re-publication of such titles as the five under review is undisputable. Most of them have been out of print for well over half a century, during which time there has been a remarkable upsurge of interest in Victorian intellectual history. Yet, for students and scholars in residence at universities constructed since the First World War, such books are virtually unobtainable. Research is accordingly hamstrung and, more important, it becomes impossible to assign to students primary sources, which, in the view of teachers like myself, are often preferable to existing secondary accounts.

Thus courses in the social thought of nineteenth century Britain would greatly benefit from having these volumes by Carpenter, Combe, Lewes, Spencer and Wallace included on their reading lists. On the question of positivism's 'curious effect' upon Victorian thinkers, one could do far worse than consult the 'Eleventh Epoch' of Lewes's *History*, "Philosophy finally relinquishing its Place in favour of Positive Science." The decline of phrenology could be traced through the works of Combe, Carpenter and Wallace. Even more fascinating would be a comparison between the diametrically opposed sociopolitical views of those two Darwinians before the name, Spencer and Wallace. The Gregg series, in short, would soon to hold great promise.

But there is a snag. Excluding the cost of *The Constitution of Man*, the price of the four remaining books comes to £31.80 ($76.40). I honestly don't understand how production costs could justify such an abnormally high figure. The volumes are unedited, facsimile offprints of works whose copyrights have long since expired. Even the bindings, serviceable though they may be, are nothing out of the ordinary. The real question, however, is: who can afford the expenditure of so much money for apparently so little in return? Presumably the libraries of newer American universities can manage such an outlay, but corresponding institutions in Britain will have to think twice (and economize elsewhere) before making their purchases. Individual scholars, on the other hand, probably fall into two categories. Those affluent enough to buy reprints at such prices can undoubtedly afford, if not the first, then at least a later edition of the original. As for the remainder of academics, myself included, acquisition of any one of the Gregg publications is financially out of the question. Needless to say, this is a great pity.

PAUL GARY WERSKEY

Prospect of Perfection

The Perfectibility of Man. By John Passmore. Pp. 396. (Duckworth: London, October 1970.) £4.20.

To some of us in these days, the idea of perfectibility in man seems perhaps a sad illusion or a sick joke. But it has been far from a joke for many earnest thinkers in the past, and it may still prove to be a quite compelling illusion for multitudes in the future. For humanity has always sought consolation in its sufferings from one illusion or another of which persuasive voices have been able to convince it; persuasive if not at all disinterested voices.

The consequences of a belief in perfectibility are therefore enough to justify Professor Passmore's inquiry into its symptoms and expression. But what is the perfectibility that is believed in? This is what he wisely refrains from telling us. It is something benevolently attainable by effort, by education, by conversion, by election, by heredity, by evolution. It is something fortunately attainable by individuals, by societies, by classes or by races. Or not attainable. It is something which the priest or the prophet or the political philosopher often judges by its effects in improving or controlling the behaviour of those who hear and obey, such effects being subject to the prevailing temper, bold and optimistic, or pessimistic and timid, of the time and place and people. For as Teilhard de Chardin wrote, and Karl Marx and many of his disciples might have written, "Men must believe that mankind is perfectible, since otherwise human effort will collapse".

Scientists no doubt often feel like that, and by taking drugs, as Professor Passmore suggests, could always feel so. But when they write they are usually more careful. They observe certain rules, but these rules have allowed them to reach conclusions which would be unbelievable had not our author most authentically collected and quoted them. When Francis Galton explains that men could be selected as superior to white men as white men are to negroes, we are surprised. When H. J. Muller more recently foresees "modes of thought and living that would today seem inconceivably godlike", we are more surprised. But what surprises us most, and most instructively, is the sentence in which Darwin almost concludes the *Origin of Species*. This is a sentence which introduces his view of perfectibility and it escaped unscathed the successive recensions of his book: "As natural selection works solely by and for the good of each being, all corporeal and mental endowments will tend to progress towards perfection".

Five years later, Alfred Russel Wallace was able to fill in the details of Darwin's picture. In his view, man would become a "single homogeneous race" corresponding in character with "the noblest specimens of existing humanity". In other words, we shall not all move forward together as Galton imagined but those behind will catch up. Trotsky, much later, was to express the same hope or faith. It was the correct view for the Marxist as well as the Darwinian.

Professor Passmore does not take the scientific argument beyond this Darwinian point. He merely concludes that although mankind may never be perfect, men (and perhaps women) might well try to do better. But it is worth our while noting how far the views of Darwin and Galton, as well as of Marx and Trotsky, might be connected with the scientific evidence available to us.

In the first place today we are faced with the collapse of Lamarckian assumptions. Their infinite scope for wish fulfilment and dictatorial exploitation, priestly and secular, is lost. This leaves the mystical and also the political perfectibilist without his old scientific ground to stand on. In the second place, our ideas about natural selection make Darwin's argument look very shaky. Today we do not see natural selection working just "for the good of each being". On the contrary, we see it often subordinating the individual to the needs of the community and the requirements of the breeding system. We also see it operating within a framework which chemically and mechanically is most refractory. For example, we have to put up with twenty-three chromosomes: is this a magic number? Is homozygosity the perfect state of man, or even of woman ?

Perhaps the most striking change in our beliefs concerns uniformity. The notion of a community or a species which is entirely without differences, individual or racial, social or sexual, implies utter stability and utter stagnation. It has always been abominable. It has now also become inconceivable. How should we get on without our genetic load ?

Where then will the perfectibilist take his last stand ? The environment would seem to be his safest refuge. Man has learnt to control his physical environment. He has indeed frequently been heard to boast of his unique powers in this respect. But as he has not learnt to control his genetic environment, which depends on his own breeding in quality or quantity, his physical accomplishment has become a destructive asset. We cannot therefore hope for a speedy millenium. But neither, fortunately, need we fear it.

Professor Passmore does not say these things. But he is sceptical enough to approve of them. The only fault in his book is that it lacks arrangement and therefore continuity. His work was not planned. It swept its author along. It turned out to be an encyclopaedia which takes him and us through the burrows and warrens of error and fraud, following each new rabbit that he uncovers and pursuing it to the last indefatigable but fatiguing footnote. It may be a long time before anybody pursues these things further or in such small print. C. D. DARLINGTON

Botanical Walkabout

Allan Cunningham: Botanist and Explorer. By W. G. McMinn. Pp. 147+4 plates. (Melbourne University: Carlton, Victoria; International Scholarly Book Services: London. December 1970.) $4.20; £2.00.

THE huge unexplored continent of Australia of the nineteenth century offering a challenging, unique flora and fauna sets the background for W. G. McMinn's study of Allan Cunningham, undoubtedly one of Australia's greatest botanical collectors. The author in his preface disclaims any attempt to assess or analyse Cunningham's scientific ability, but on the other hand makes no apology for offering a study of the man. Although Allan Cunningham is portrayed with great sympathy and feeling the effect is a rather formal historical work containing considerable information on early exploration in Australia.

The author shows excellent insight into the mind and character of the systematic naturalist, and readers from disciplines other than botany may be interested and enjoy this study. As a readable botanical narrative, however, it is a disappointment, for little use is made of Cunningham's detailed and fascinating botanical journals. In comparison with Ida Lee's *Early Explorers in Australia*, I feel there is a lack of balance between explorer and botanist.

The introductory chapters read well, describing Allan Cunningham as an insecure young man lacking in self assurance, attributable to his rather humble background. Following his contact with and commission by Sir Joseph Banks to make botanical collections for Kew, his confidence gradually grew into scholarly diffidence and quiet unexpansiveness. Later chapters outline his exploration, detailing, perhaps too fully, his travels and recounting his thoughts, activities and achievements as a botanical collector but superficially. The gradual growth of confidence with experience and success turned, with failing health, to disillusionment and discontent. Some of the journeys could have been presented more clearly by the inclusion of more and better maps.

In the final chapter the author, in summarizing Cunningham's character, comments on his diligence and industry by referring to the tireless walks in search of orchids, and his careful follow up of the results achieved at Kew with his seeds and seedlings; and on his sensitivity by reference to his writing on *Acacia podolyriaefolia*. These generalizations, although undoubtedly derived from Cunningham's journals, are insufficiently exemplified in the principal part of the work. It is a pity that McMinn did not expand the botanical aspect of this study a little more fully, because as a result one is left with a feeling that the work lacks depth. The extensive references and bibliography clearly indicate exhaustive research and will be undoubtedly of value to the student.

I. K. FERGUSON

Freshwater Sediments

Non-Marine Organic Geochemistry. By Frederick M. Swain. (Cambridge Earth Science Series.) Pp. xii+445. (Cambridge University: London, October 1970.) £10.00; $32.50.

THIS volume gathers together many data on the nature and variation of organic matter in freshwater sediments that will be of use to organic geochemists working in widely differing fields. The book is, however, a good illustration of the difficulties—even for an experienced and well-regarded scientist—of writing a balanced, comprehensive review of a scientific field, which, if not undergoing explosive expansion, is certainly developing with vigour. Dr Swain's new book does not change the view that up to now the edited book, with chapters by a number of authors, has been the more successful presentation in the detailed discussion and evaluation of the different facets of organic geochemistry.

The first chapter of *Non-Marine Organic Geochemistry* is a necessary survey of organic materials in the geological environment, which is unfortunately marred, as are other chapters, by numerous errors in structural formulae. The more authoritative parts of the book, the chapters on bitumens, protein amino-acids, carbohydrates and organic pigments of non-marine sediments, comprising almost half of the text, rely heavily on the researches of Swain and his co-workers. These chapters carry most critical comment, although more contrasts could usefully have been made with, for example, the character and behaviour of organic materials in other environments. Chapters on field and laboratory analysis of organic materials and on the characteristics of non-marine sediments are also considerably influenced by the author's work. Away from Swain's chief interests, the book becomes much more a matter of report. The chapter on non-marine coals is weak, and so unbalanced in form and content that the contribution is misleading. Furthermore, many of the coals considered, particularly those of the paralic coalfields, must certainly have been at least partly influenced by marine or near-marine conditions. The book also contains appendices giving solvent systems and R_f values for paper and thin-layer chromatography, thirty pages of references and adequate subject and author indices.

The editors must exert more control on their printers to ensure a higher quality of production in the rest of the series. Absorption spectra should not overlap figure margins. The smudging and persistent variation on many pages of the ink density of chemical formulae and resonance structures of benzene should not have been allowed, and the quite inexplicable changes in type width give what must surely be an unintended significance to certain chemical reactions. These deficiencies are, however, chiefly in the first fifty pages of the text, and the general impression of type and figure lay-out of the volume is pleasing.

DUNCAN MURCHISON

Drug Data

Sympathomimetic Drugs. By Domingo M. Aviado. (A Monograph in the Bannerstone Division of American Lectures in Anesthesiology.) Pp. xix+613. (Thomas: Springfield, Illinois, July 1970.) $40.

THIS book has been compiled for medical students, postgraduate students and doctors. It aims to assist doctors whether working in hospital or outside. Owing to the pruning of the time available for teaching pharmacology to medical students in Philadelphia, USA, the text deals less with general pharmacological principles arising from extensive courses in practical pharmacology, and more with clinical uses. Because of this pressure of circumstance, the author plunges the reader into the deep end, dealing in detail in chapters 1 to 5, 7, 8 and 10 with eight of the sympathomimetic drugs most commonly used in the US, namely epinephrine (adrenaline), norepinephrine (noradrenaline), ephedrine, metaraminol, mephentermine (mephenteramine), phenylephrine, methoxamine and isoproterenol (isoprenaline). To UK eyes, this list may seem somewhat strange, but it serves to emphasize that there are national differences when considering the emphasis placed on various drugs by the user communities. Chapters 6, 9 and 11 consider much wider spectra of drugs which might be used for raising blood pressure, cardiac stimulation, nasal decongestion and appetite suppression, vasoconstriction, vasodilation and relaxation of the bronchiolar muscle, against the detailed background information provided for each of the eight archetype sympathomimetic compounds. Each chapter is followed by a short summary of its main points and a substantial reference list.

This type of approach in a textbook would seem to be more useful to the British medical graduate than to the undergraduate, although the latter is invited to start by reading chapter 12 entitled "Pharmacology of Sympathomimetic Drugs" before turning to consider the foregoing chapters. Chapter 12 will enable him "to learn . . . the uses of sympathomimetic drugs in therapeutics". This phrase sums up the approach which is essentially directed towards the practical.

Chapter 12 deals in detail with the pharmacological anatomy and physiology of the sympathetic system before turning to consider α and β receptors and α and β blocking agents. The brief and rather superficial treatment of α and β receptors is disappointing in a book running to over 600 pages, which might be expected to give a wide perspective of its subject. The β blocking agent propranolol receives only passing reference on one page in its own right, and is mentioned on three other pages when referring to interactions with other drugs. Practalol receives no mention. The author, however, devotes much effort to grouping sympathomimetic drugs in Chapter 12 under four headings relating to a direct or indirect action on α and β receptors stimulating the heart and influencing the blood vessels, or acting directly on α receptors (chiefly to constrict blood vessels) or on β receptors (to dilate blood vessels and to relax smooth muscle). He goes on to provide examples of eight clinical situations in which sympathomimetic drugs may be required, ranging from an anaphylaxis, through cardiac stimulation, bronchodilatation and mydrias to combating shock. The practical approach shows up to great advantage here because the dose and route of administration of each of (often many) alternative drugs are given together with reference to other pages in the book on which the drug is treated in more detail. This type of readily available and systematized practical information is often missing from standard UK textbooks.

Professor Aviado has produced a substantial volume with many references which makes for an unusual presentation of sympathomimetic drugs. He has disciplined himself to take a strict approach severely directed to clinical applications. If the reader is prepared to use the book as a source of such information, he will find much to interest him. No fewer than 386 compounds are tabulated in the final chapter (13). These include the eight considered in detail and 53 in lesser detail in the preceding chapters. In spite of this long list, practalol has escaped inclusion. If the reader is, however, seeking a deep understanding of the mode of action of sympathomimetic drugs, then he will not find the volume helpful for this purpose but he will find the encyclopaedic list of compounds helpful in tracing the structure of less well known compounds.

The author, in his approach, poses the question "what sort of a book is required" by the medical student and graduate and others working in ancillary fields—a volume answering a host of practical questions or one blending an information source with an understanding of the underlying principles? He is courageous to undertake this task, which will stimulate us to consider our values and requirements in textbooks in this field with particular reference to the growing needs in the UK for extensive educational programmes for postgraduate medical practitioners, young and old alike.

J. P. QUILLIAM

Probing the Brain

Physiological Psychology. By Peter M. Milner. Pp. x+531. (Holt, Rinehart and Winston: New York and London, 1970.)

THE view that the royal road of advance in physiological psychology involves finding out what happens to an animal's behaviour when one prods around inside its head is widespread. Peter Milner, whose book is the most recent addition to texts on the subject, is evidently of this persuasion and states that "the logic of probing the nervous system for cues (*sic*) to behaviour is almost universally accepted".

The author explains that he is interested in understanding behaviour in the same way that it is possible to understand a motor car or a radio. The difficulty about the probing approach—of which he approves—is that valuable insights about the workings of a radio are not gained by observing its behaviour while thrusting a hot soldering iron into its innards. Even poking about with the terminals of a voltmeter is not going to be much good if we do not already understand how the radio works and what to look for. Comprehending the principles upon which brain mechanisms operate seems to require techniques (such as simulation) which are of a quite different kind.

What one gets from probing is the strong impression that the brain has something to do with behaviour, together with a set of notions about particular parts of the brain being concerned in particular aspects of behaviour. Though much of physiological psychology is still at this stage, the time has come to get away from this kind of approach. Milner makes a modest attempt to do so in that, within the contexts of sensory and motivational systems, he gives a small amount of space to the discussion of possible mechanisms and models. Unfortunately, he does not take this nearly far enough, either in extent or rigour.

This book is one of half a dozen or so such texts available, and is not a bad example of its kind. The author traverses the (by now) familiar field, but does take the trouble to describe most of the experiments that he mentions in sufficient detail for the reader to be able to grasp what was done, and he does adopt a more critical approach than some of his competitors.

KEITH OATLEY

Brain Histochemistry

Macaca mulatta: Enzyme Histochemistry of the Nervous System. By Sohan L. Manocha and Totada R. Shantha. Pp. xii + 348. (Academic: New York and London, August 1970.) £10.05.

THIS work is based on the histochemistry of material from twelve monkeys. The oxidative (monoamine oxidase, succinic and lactic dehydrogenase) and hydrolytic (acid and alkaline phosphatase, ATPase, simple esterase, true and pseudo-cholinesterase) enzymes are investigated using fresh frozen sections. The regions examined include the cerebral cortical areas, the hippocampus, basal ganglia, diencephalon, brain stem, cerebellum, spinal cord, dorsal root ganglia, olfactory bulb, retina, optic nerve and other eye parts, choroid plexus, ependyma and peripheral nerve perineurium. With some two hundred and fifty three micrographs (no electron micrographs) the text is well illustrated although a number of the plates look rather fuzzy—perhaps indicating a need for thinner sections. The material is well laid out, and the introduction to the methods employed should be clearly comprehensible to the novice. The book could well serve as an introduction to brain histochemistry, for the findings are related to numerous references to the literature on corresponding regions in other species (the references stop short, though, at 1968).

Investigators who have kept up to date with the literature in brain fine structure and the localization of transmitter substances will, however, find the discussions disappointing, for in many places the authors seem to have little grasp of these very relevant topics. In the cerebral cortex, for example, they are unaware that most synapses are located on dendritic spines, and that there is growing evidence that (in pyramidal cells) these have an excitatory transmitter. On the other hand, somatic contacts may have mostly inhibitory chemically mediated synapses. The literature on transmitters in the subformical organ has not really been explored. The presence of choline esterase in dorsal root ganglion cells known to be noncholinergic could have been discussed at much greater length. The cerebellar glomeruli not only contain mossy fibre contacts but a second set—the Golgi cell granule dendrite contacts. The former are excitatory and the latter are inhibitory. Thus we have a dual system which can be precisely pinpointed with the microscope—is it any wonder that the histochemistry of the cerebellar cortex is in such a state of chaos when topics like this are ignored?

E. G. GRAY

Identifying Yeasts

The Yeasts: a Taxonomic Study. Edited by J. Lodder. Second edition, revised and enlarged. Pp. xvi + 1,385. (North-Holland: Amsterdam and London, 1970.) £27.40.

"THE main intention of this work," says Lodder, "is to produce a book for identifying yeasts." Indeed, anybody now wanting to identify yeasts must have it constantly on his laboratory bench. The fourteen authors, who include most of the leading yeast taxonomists, have apportioned the genera among themselves. For this unique book, they have examined 4,300 strains and classified them into 39 genera and 349 species. Each species is described extensively: the macro- and microscopical appearance, the life cycle (if known), the ability to use 30 or 40 organic compounds as sole sources of carbon for aerobic growth ("assimilation"), 5 to 13 of them for semi-anaerobic "fermentation" and some additional physiological tests. The account of each species includes the number of strains examined, their sources and some information about how they vary, one from another. There is an invaluable bibliography for each chapter, and the book has a comprehensive index to the names of taxa which makes it easy to find the currently accepted synonym for almost any yeast. There is no general index.

I propose to discuss the book principally as one using it for identifying yeasts, and not to review the detailed classification. The accepted primary division of the yeasts is into those that do and those that do not form ascospores. In his chapter on methods, Walt says "In view of the importance of ascospore formation as a taxonomic criterion, a strain may only be regarded as anascosporogenous when (a) it has failed to yield ascospores on a wide variety of media; (b) it has been shown not to be a haploid mating type of some or other heterothallic species." Walt lists fourteen ascogenic media. When one is faced with hundreds of strains to identify, using even half these media may be a formidable task; after inoculation they must be examined with the oil immersion objective at three days and then weekly "for at least 4–6 weeks", unless ascospores have been seen. Even after this, a negative result is equivocal. Recently, a colleague and I isolated and identified nearly 1,000 yeasts; as over 800 were (anascosporogenous) *Cryptococci*, it would have been futile to have tested them for ascospore formation.

Although ascosporulation is important in classification, formation of ascospores need not be made important in identification. An alternative to Lodder's identification key could be based primarily on growth and fermentation tests. Microscopical appearance, and even ascosporulation, could then be used for confirmation of identity and for distinguishing between species with the same responses to the physiological tests.

The nutritional tests must, of course, be uniformly carried out. On this Lodder is sanguine: "With certain minor exceptions . . . identical methods were used for every standard description, so that the individuality of each observer should not have significant effects on the results of the tests." Nevertheless, Walt refers to several methods that can be used. Though he evidently favours unshaken tubes of liquid media for growth tests, I found no statement that these were used by all the authors. The exact method of testing may not affect results when the yeast grows either well or not at all; but, even when aeration is not a limiting factor, the utilization of many test compounds often involves lags of up to several days (not a consequence of selection) and doubling times of as long as twenty hours. Such slow responses are particularly sensitive to test conditions. Hence the reaction of a given strain to one substrate may be described by different authors as positive, slow, weak or even negative. Accordingly, a new key derived from this book might use three categories of test response: positive, negative and query; the last would include all equivocal responses and those varying between strains of one species.

Compared with the first edition, written by Lodder and Kreger-van Rij and published in 1952, more than three times as many strains have been classified into over twice the number of species. The number of physiological tests has been increased from 15 to between 40 and 60, depending on the genus. The description of each species in the first edition included excellent drawings which greatly help identification; unfortunately in the second edition a number of species are illustrated sparsely or not at all.

Although the book is unwieldy, it is convenient as a single volume. Its high price will stop many buying their own copies, but the amount of information justifies the cost to any laboratory concerned with yeasts. The wealth of information about the capacities of all known kinds of yeast to utilize many organic substrates, combined with the summaries of the life cycles, is potentially of great industrial interest. It could also be an important basis for much research in microbial physiology and genetics.

JAMES A. BARNETT

CORRESPONDENCE

PhD Theses

SIR,—Every university library in the country contains scores of PhD theses, each representing three years of full-time research financed by government or industry and three years' supervision by a member of the university staff as well as accessory technical assistance and consumable equipment. The return for the several thousands spent per PhD is a thesis on the library shelf and a piece of paper for the candidate which ensures that he will command a higher salary than he could otherwise expect.

This seems unnecessarily and excessively expensive in view of the fact that although these theses are theoretically available for consultation, the difficulties encountered in attempting to refer to them verge on the insurmountable, and the scientific community thus does not benefit from the work.

An essential part of training in research should be preparation for publication, yet the PhD candidate is allowed to indulge in a verbose expansiveness that no editor of a scientific journal would contemplate for a moment.

PhD theses should consist of work written up in the form of papers which, if they are not already published, should at least have been accepted by a reputable journal. (As is the practice with certain learned societies, the raw data on which conclusions are based may be deposited in suitable archives.) In this way a return for the large financial outlay will be guaranteed and the candidates will be trained to conduct research realistically. Furthermore, examiners will no longer be obliged to spend hours plodding through inordinate reams of rubbish to extract the few kernels of new and useful information.

My own students write directly for publication, which not only spurs their efforts during the research but saves them from the trauma of "writing up" during their last few months in the department. At the end of this, the idea of going through the thesis extracting the publishable parts and rewriting them for publication is so abhorrent that in most cases it is never accomplished.

Although in many universities it is possible to present papers alone for a PhD, there is resistance to this from both academic and administrative staff. Yet in a situation where two equally qualified applicants for a post have both submitted for a PhD—applicant A a normal thesis, applicant B papers—there is little doubt that B will be selected.

On the grounds of cost-effectiveness, obligation to the scientific community and self-interest of the candidate, the present system of preparing PhD theses should be discarded at the earliest opportunity.

Yours faithfully,

L. BEVERLY HALSTEAD

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Dowsing

SIR,—The current (January) number of *Theoria to Theory* contains an interview with Colonel Merrylees, a past president of the British Society of Dowsers, in which he talks among other things about his selection of young men for sensitivity in dowsing at an army establishment. This work has been the subject of destructive criticism in an article in *Nature* (**229**, 163; 1971). A comment on the attack in *Nature* will be published in the ensuing number of *Theoria to Theory* (April).

Yours faithfully,

DOROTHY EMMET

Editor,
Theoria to Theory,
9 Marion Close,
Cambridge

Obituary

Professor A. Ghigi

ALESSANDRO GHIGI, professor emeritus of the University of Bologna, who died in Bologna on November 20, 1970, in his ninety-sixth year, was born in that city in 1875. He was held in very high esteem in Italy, and was a member of the Pontificia Accademia delle Scienze and the Accademia Nazionale dei Lincei and also of the Accademia delle Scienze of Bologna, Torini and Modena, and many scientific societies in other countries. He was awarded honorary doctorates at the Universities of Boston and Coimbra.

His long and distinguished career encompassed many aspects of zoology; from 1902 to 1915 he was lecturer in zoology and agricultural entomology in the School of Agriculture of the University of Bologna, and subsequently lecturer in zoology and comparative anatomy in the University of Ferrara from 1904 till 1908, when he became professor, a position he held until the end of 1922. That year he was appointed to the chair of zoology at the University of Bologna, where he became Rector in 1930, a position he held for the unprecedented period of thirteen years. He directed the Institute of Zoology of the University which he established for almost thirty years, and which attained a high reputation both for its scientific and teaching standards.

He laid the basis of practical aviculture in Italy, which previously had been completely neglected, and also founded the Institute of Aviculture in Bologna. He was very interested in these subjects, and became Honorary President of the World Poultry Science Association. He was also a leading authority on ornamental pheasants and guinea-fowl. He studied the problems of game animals in relation to hunting, and contributed much biological information by the institution of observations on migration and the establishment of a laboratory of applied zoology concerning game animals, including birds.

Ghigi made several zoological expeditions: to Cyrenaica in 1920; the Dodecanese Islands in 1926; Tehuantepec, Mexico, in 1927; Morocco in 1930; and Lake Chapala and Patzcuaro, Mexico, in 1932; on which he collected numerous species, several new to science. His publications, of which there are more than 350, cover a wide range of subjects on various aspects of zoology including morphology, genetics and systematics, and deal with mollusca, crustacea, insects, mammals and especially birds.

He made a great contribution to the conservation of wild life, both nationally and internationally, and undoubtedly did more than any single individual to secure a better preservation of wild birds in Italy. He was a vice-president of the International Council for Bird

Preservation from 1954–1966, and chairman of the Italian National Section for thirty-five years, only relinquishing this position in 1970 on account of ill health, when he was immediately elected honorary president of the section.

Ghigi was a great traveller until just before he died, and attended many international conferences. In 1968, at the age of 94, he attended a conference in Venezuela in March, followed by another in Hungary in May, and a third in Rumania in June. Ghigi was an outstanding personality wherever he went, and he will be mourned all over the world.

Academician A. I. Mikoyan

ACADEMICIAN Artem Ivanovich Mikoyan, one of the leading aircraft designers of the Soviet Union, died on December 9, 1970.

Mikoyan was born in 1905, in the village of Sanain, in Armenia. He was educated at the Zhukovskii Air Force Engineering Academy. In 1937 he became head of the design department of the experimental aircraft design bureau, and subsequently rose to be chief designer and director. In 1945, he visited Germany to study German aircraft construction methods. He was elected to the Academy of Sciences as a Corresponding Member in 1953. Together with M. I. Gurevich, he designed the series of MiG fighter aircraft. His first design for a turbojet aircraft was completed in 1946. From 1954 onwards he designed numerous types of supersonic aircraft.

For his services to the aircraft industry, Mikoyan received three Stalin Prizes (now State Prizes), one Lenin Prize, the Order of Lenin (5 times), four other Orders and a number of medals. He was twice nominated as a Hero of Socialist Labour.

Announcements

University News

Professor W. Keasley Welch, University of Colorado, has been appointed Ingraham professor of neurosurgery at **Harvard University** and neurosurgeon-in-chief at the Children's Hospital Medical Center.

Appointments

Dr Kendrick W. Hare has been appointed director of the **Pakistan-SEATO Cholera Research Laboratory** in Dacca, in succession to **Dr Robert A. Phillips.**

Miscellaneous

Dr Stephen J. Smith, acting chief of the Laboratory Astrophysics Division of the US National Bureau of Standards, has been elected chairman of the **Joint Institute for Laboratory Astrophysics** for 1971 and 1972.

Dr William R. Busing, Oak Ridge National Laboratory, has been elected president of the **American Crystallographic Association** for 1971, in succession to **Dr David P. Shoemaker,** Oregon State University. **Dr Jerome Karle,** US Naval Research Laboratory, has been elected vice-president.

Professor Abdus Salam, director of the International Centre for Theoretical Physics, Trieste, and professor of theoretical physics at Imperial College, London, has been awarded the **J. Robert Oppenheimer memorial prize** of the University of Miami, in recognition of his work in quantum electrodynamics and elementary particle physics.

The council of the **Geological Society of London** has announced the following medal awards for 1971: **Wollaston Medal,** to **Brigadier R. A. Bagnold,** for his contributions to the science of sand movement and its application to sedimentology and engineering problems; **Murchison Medal,** to **Professor B. C. King,** for his contributions to petrology and African geology; **Lyell Medal,** to **Professor P. Allen,** for his work in sedimentology; **Bigsby Medal,** to **Dr F. J. Vine,** for his contributions to the understanding of the evolution of the ocean floor. The proceeds of the Murchison Fund have been awarded to **Dr J. Dewey,** for his contributions to the understanding of the Lower Palaeozoic of the North Atlantic Province. Moieties of the Lyell Fund have been awarded to **Dr G. Evans,** for his work on recent coastal sedimentation, to **Dr J. M. Hancock,** for his work on the Cretaceous rocks of the British Isles, and to **Mr T. R. Owen,** in recognition of his services in the teaching of geology.

The recipients of the **1970 National Medal of Science,** awarded by the US Government for distinguished achievement in science, have been announced: **Professor R. D. Brauer,** Harvard University; **Professor Robert H. Dicke,** Princeton University; **Barbara McClintock,** Carnegie Institution of Washington; **George E. Mueller,** General Dynamics Corporation; **Albert B. Sabin,** Weizmann Institute of Science, Rehovoth; **Allan R. Sandage,** Carnegie Institution of Washington; **Professor John C. Slater,** University of Florida; **Professor John A. Wheeler,** Princeton University; and the **late Professor Saul Winstein,** University of California

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British Diary

Monday, February 22

Concorde (6.30 p.m.) Mr B. Trubshaw, Institution of Electrical Engineers, London Graduate and Student Section, jointly with I.Mech.E., at 1 Birdcage Walk, London SW1.

Semiconductor Nuclear Devices (2.30 p.m. colloquium) Institution of Electrical Engineers, at Savoy Place, London WC2.

Tuesday, February 23

Cable Installations Designed by Computer Techniques (5.30 p.m. discussion) Institution of Electrical Engineers, at Savoy Place, London WC2.

Experiences with Electrostatic and Mechanical Dust Collectors (6 p.m. discussion) Institution of Mechanical Engineers, at 1 Birdcage Walk, London SW1.

Faraday and the Beginning of Useful Electricity (3 p.m.) Professor R. King, Royal Institution, at 21 Albemarle Street, London W1. (Lecture for Preparatory School Pupils from Schools in London and the Home Counties. To be repeated on February 24 and 25.)

Respiratory Viruses (5.30 p.m.) Dr D. A. J. Tyrrell, University of London, at the Institute of Child Health, 30 Guilford Street, London WC1. (Fourteenth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

The New Anthropology and Its Critics (5 p.m.) Mr Edwin Ardener, University of London, at the London School of Economics and Political Science, Houghton Street, London WC2. (Malinowski Memorial Lecture.)

Wednesday, February 24

Built-in Test Equipment for the Concorde (6 p.m. discussion) Institution of Electrical Engineers, at the Royal Aeronautical Society, 4 Hamilton Place, London W1.

Culpeper's Herbal: Over Three Centuries (1 p.m.) Dr F. N. L. Poynter, Royal Institution, History of Science Discussion Group, at 21 Albermarle Street, London W1.

Environment of Packages in Transit (2.30 p.m. symposium) Society of Environmental Engineers, in the Mechanical Engineering Department, Imperial College, London SW7.

Food Additive Specifications (6.15 p.m.) Dr H. Egan, Society of Chemical Industry, Food Group, at 14 Belgrave Square, London SW1.

Long Distance Waveguides (6.30 p.m.) Mr N. Lacey, Institution of Electrical Engineers, London Graduate and Student Section, at Croydon Technical College, Fairfield, Croydon, Surrey.

Muscles as Machinery (5.30 p.m.) Professor D. R. Wilkie, University of London, in the Botany Theatre, University College London, Gower Street, London WC1.

New Sources of Power for Industry (6 p.m.) Mr Arthur Palmer, MP, Royal Society of Arts, at John Adam Street, Adelphi, London WC2.

New Views on Sleep and Dreams (6.30 p.m.) Dr C. R. Evans, Institution of Electrical Engineers, at King Edward VI Grammar School, Broomfield Road, Chelmsford, Essex.

Recent Developments in Nucleonic Instruments used for Industrial Process Control (6 p.m.) Mr J. F. Cameron, Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

The Determination of Trace Elements in Metallurgical Products (2.30 p.m.) Society for Analytical Chemistry, at Lanchester Polytechnic, Coventry.

Thermal Effects in Liquid Phase Reactions (2.30 p.m.) Mr W. S. Sebborn, Society for Analytical Chemistry, at the University of Essex, Colchester, Essex.

Video Recording (7 p.m.) Mr A. H. Jones, Institution of Electrical Engineers, at the Star and Garter Hotel, Dorking, Surrey.

Wind Pressure Effects on Structures (6 p.m.) Mr C. Scruton, Institution of Mechanical Engineers, at 1 Birdcage Walk, London SW1. (James Clayton Lecture.)

Thursday, February 25

Application of Micro Fragrances (7.30 p.m.) Mr R. H. Sudekum, British Society of Perfumers, at the Royal Society of Arts, John Adam Street, London WC2.

Application of the Code of Practice for the Protection of Persons Exposed to Ionizing Radiations, Mr J. M. Rees; **The Radioactive Substance Act 1960,** Mr R. G. D. Osmong; **Design of Radiochemical Laboratories in Universities,** Mr E. I. Hamilton (2.30 p.m.) Society for Analytical Chemistry, at the Wellcome Building, 183 Euston Road, London NW1.

Art and Science: 7. Abstract Art and the Sub-atomic Universe (1.30 p.m.) Mr P. D. Carpenter, University of London, at Imperial College, London SW7.

Changes and the Future in Electrical Engineering (5.30 p.m.) Mr S. Z. de Ferranti, Institution of Electrical Engineers, at the Central Hall, Westminster, London SW1. (Faraday Lecture.)

Legal Aspects of Radiochemistry (2.30 p.m.) Society for Analytical Chemistry, Radiochemical Methods Group, at the Wellcome Building, 183 Euston Road, London NW1.

Management Development in Theory and Practice (6 p.m.) Mr J. Mardon, Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

Nine Delhis (5.15 p.m.) Mr Patwant Singh, Royal Society of Arts, Commonwealth Section, at John Adam Street, Adelphi, London WC2.

Node Logic (7.30 p.m.) Mr B. S. Walker, Institution of Electronic and Radio Engineers, at the J. J. Thomson Laboratory, University of Reading, Whiteknights Park, Reading.

Properties of Waves. Young and the Wave Theory of Light (1 p.m. films) Royal Institution, at 21 Albemarle Street, London W1.

Red Cells and their Enzymes (5.30 p.m.) Professor T. A. J. Prankerd, University of London, at the Institute of Child Health, 30 Guilford Street, London WC1. (Last of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

Satellite Communications: Future and Trends (6.30 p.m.) Mr J. Brown, Institution of Electronic and Radio Engineers, at the University Engineering Laboratories, Trumpington Street, Cambridge.

Television Communication by Satellite and Conventional Systems (7 p.m.) Mr D. J. Whyte, Institution of Electronic and Radio Engineers, at Medway College of Technology, Chatham, Kent.

Use and Re-Use of Water in Industry (6.15 p.m. symposium) Society of Chemical Industry, Food Group, at 14 Belgrave Square, London SW1.

Friday, February 26

Effective Contraceptive Services (9 p.m.) Dr Ian A. G. MacQueen, Royal Institution, at 21 Albemarle Street, London W1. (The Woodhull Lecture.)

Laser Research at the National Physical Laboratory (1 p.m.) Mr J. W. C. Gates, Royal Institution, Photochemistry Discussion Group, at 21 Albemarle Street, London W1.

The Glass Transition Temperature of Paint Films (7.15 p.m.) Mr J. L. Prosser, Oil and Colour Chemists' Association, at the Angel Hotel, Cardiff.

Saturday, February 27

Mountain Bushmen of Eastern Lesotho—Their Art and Archaeology (3.30 p.m.) Miss Patricia Vinnicombe and Mr Patrick Carter, Inner London Education Authority, at the Horniman Museum, London Road, Forest Hill, London SE23.

Monday, March 1

How to Enjoy Food Additives (6.30 p.m.) Professor B. C. L. Weedon, Society of Chemical Industry, London Section, jointly with the Food Group, at 14 Belgrave Square, London SW1.

Telecommunications—New Practices, Old Concepts (5.30 p.m.) Professor J. Greig, Institution of Electrical Engineers, at Savoy Place, London WC2.

The Use of Computers in Aircraft (7 p.m.) Mr B. J. Calvert, Institution of Electrical Engineers, at the Royal Star Hotel, Maidstone, Kent.

Reports and Publications

not included in the monthly Books Supplement

Great Britain and Ireland

British Medical Bulletin, Vol. 27, No. 1, (January 1971): Symposium on Epidemiology of Non-Communicable Disease. Pp. 1–94. (London: British Council, 1971.) £2. [41

The Zoological Record. 1966, Vol. 103, Section 13: Insecta. Prepared by the Commonwealth Institute of Entomology and The Zoological Society of London. Pp. xvi+417. 1968, Vol. 105, Section 4: Coelenterata. Compiled by the Staff of the Zoological Society of London. Pp. iv+39. £1. 1968, Vol. 105, Section 7: Brachiopoda. Compiled by Margaret O'Hanlon. Pp. iv+24. £1. 1968, Vol. 105, Section 8: Bryozoa (Polyzoa) and Entoprocta. Compiled by Eileen Hatton. Pp. 24. 1968, Vol. 105, Section 17: Reptilia. Compiled by David Cole. Pp. vi+74. £2. (London: The Zoological Society of London, 1970.) [41

Yorskhire Flooding—Some Effects on Man and Nature. By J. Radley and C. Simms. Pp. 28. (York: Sessions Book Trust, The Ebor Press, 1971.) 50p. [41

Ministry of Transport: Road Research Laboratory. RRL Report LR 369: Air-Photograph Interpretation for Road Engineers in Britain. By Dr M. J. Dumbleton and G. West. Pp. 24. (Crowthorne, Berkshire: Road Research Laboratory, 1970.) [41

Bulletin of the British Museum (Natural History). Geology. Vol. 19, No. 6: Scottish Callovian and Oxfordian Ostracoda. By R. C. Whatley. Pp. 297–358+15 plates. £4.80. Vol. 19, No. 8: The Lower Palaeozoic Stratigraphy and Faunas of the Taurus Mountains near Beysehir, Turkey. 1: Stratigraphy. By W. T. Dean and O. Monod. Pp. 411–426. 65p. Zoology. Vol. 20, No. 4: A Review of the Species of *Hemilepistus* S.Str. Budde-Lund, 1885 (Isopoda, Porcellionidae). By R. J. Lincoln. Pp. 109–130. 80p. Vol. 21, No. 1: Decapod Crustacena Larvae collected during the International Indian Ocean Expedition. Families Raninidae and Homolidae. By A. L. Rice. Pp. 1–24. 85p. (London: British Museum (Natural History), 1970.) [41

Fabian Tract No. 404: A Social Democratic Britain. By Anthony Crosland. Pp. 16. (London: Fabian Society, 1971.) 15p. [51

Bulletin of the British Museum (Natural History). Geology. Vol. 19, No. 5: Two Upper Cretaceous Salmoniform Fishes from the Lebanon. By Colin Patterson. Pp. 205–296+5 plates. £3.90. Zoology, Vol. 20, No. 7: The Species of *Macrophthalmus* (Crustacea: Brachyura) in the Collections of the British Museum (Natural History). By R. S. K. Barnes. Pp. 203–251. £1.40. (London: British Museum (Natural History), 1970.) [51

Royal Observatory Annals No. 5: Catalogue of Stars within twenty-five parsecs of the Sun. By Sir Richard Woolley, Elizabeth A. Epps, Margaret J. Penston and Susan B. Pocock. Pp. 227. (Herstmonceux, Sussex: Royal Greenwich Observatory, 1970.) £4.40 net. [51

University of Cambridge—Department of Agricultural Science and Applied Biology Memoirs. No. 42: A Summary of the papers published and research in progress by the members of the Department and its Associated Research Organizations during the period 1 October 1969–30 September 1970. Review Series No. 25: Research in Animal Nutrition, 1950–1970. Pp. 25. (Cambridge: The University, 1970.) 15p. [71

Wildfowl 21. Edited by G. V. T. Matthews and M. A. Ogilvie. Pp. 160+16 plates. (Slimbridge, Gloucester: The Wildfowl Trust, 1970.) £1.25. [81

De Beers Diamond Research Laboratory. Diamond Information L22: Grinding with Diamond Abrasives, Part 1—Steel. By Dr Henry B. Dyer. Pp. 15. Diamond Information L23: Grinding with Diamond Abrasives, Part 2—Tungsten Carbide. By F. Hughes. Pp. 24. (London Industrial Diamond Information Bureau, 7 Rolls Buildings, EC4, 1971.) *gratis*. [81

Nuffield Committee for the Advancement of Medicine—Annual Report 1969. (Supplement No. 1 to the *University Gazette*, Vol. ci, November 1970.) Pp. 17. (Oxford: The University, 1970.) 40p. [111

Building Research Station Digest, No. 125: Colourless Treatments for Masonry. Pp. 3. (London: HMSO, 1971.) 5p. [111

Physiological Plant Pathology, Vol. 1, No. 1, January 1971. Pp. 1–82. Volume 2, 1971, 4 issues. Inland £7 plus £0–40 postage ; Abroad $19 plus $0.50 postage. (London and New York: Academic Press, 1971.) [111

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BBC Handbook 1971. Pp. 272. (London: BBC, 1971.) 50p. [131

Women in the Factory: a Study of Job Satisfaction and Labour Turnover. By Ray Wild and Dr A. B. Hill. Pp. 96. (London: Institute of Personnel Management, 1971.) £1.50. [131

Ministry of Agriculture, Fisheries and Food. Technical Bulletin No. 18: Manual of Veterinary Parasitological Laboratory Techniques. Pp. vi+131 +7 plates. (London: HMSO, 1971.) 90p net. [141

NLL Announcement Bulletin: a Guide to British Reports, Translations and Theses, Vol. 1, No. 1, January 1971. Pp. 1–50. (Walton, Boston Spa: National Lending Library for Science and Technology, 1971.) [141

Universities Research Reactor—Annual Report 1969/1970. Pp. vii+29. (Warrington, Lancs: Universities Research Reactor, 1971.) [141

Jubilee Report of the Welsh Plant Breeding Station, 1919–1969. Pp. 236. (Plas Gogerddan, near Aberystwyth: Welsh Plant Breeding Station, 1970.) 50p. [141

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University of Manchester Institute of Science and Technology. Annual Report 1969/1970. Pp. 101. (Manchester: UMIST, 1971.) [151

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Neurosciences Research Program. Bulletin, Vol. 8, No. 4 (September 1970): Macromolecules in Synaptic Function—a Report based on an NRP Work Session. By Floyd E Bloom, Leslie L. Iversen and Francis O. Schmitt. Pp. 325–455. (Brookline, Mass.: Neurosciences Research Program, 280 Newton Street, 1970.) $10 (private individuals who certify that subscription is for their personal use). $20 (libraries, research units and other multiple-readership groups). [2912

Unesco. Annual Summary of Information on Natural Disasters, No. 3, 1968. Pp. 72. (Paris: Unesco ; London: HMSO, 1970.) 10 francs ; 75p ; $2.50. [2912

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Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 69–52: Preliminary Notes on the Hurwitz Group. Padlei Map—Area, Northwest Territories. By R. T. Bell. Pp. vi+13. $1.50. Map 900A: Principal Mineral Areas of Canada. Twentieth edition. (Ottawa: Queen's Printer, 1970.) [2912

Occasional Papers of the California Academy of Sciences. No. 82: Catalog of Specimens in the Type Collection of the Department of Geology, California Academy of Sciences. Cephalopoda. By Victor A. Zullo and Leo G. Hertlein. Pp. 130. No. 83: The Genus *Enlinia* Aldrich in America North of Mexico (Diptera: Dolichopodidae). By Harold Robinson and Paul H. Arnaud, Jr. Pp. 9. No. 84: A New Species of the Genus *Platymantis* (Ranidae) with a List of Amphibians Known from South Gigante Island, Philippines. By Walter C. Brown and Angel C. Alcala. Pp. 8. Proceedings of the California Academy of Sciences, Fourth Series. Vol. 37, No. 13: On the Diet and Feeding Behaviour of the Northern Anchovy *Engraulis mordax* (Girard). By Anatole S. Loukashkin. Pp. 419–458. Vol. 37, No. 14: *Polydora alloporis*, New Species, a Commensal Spionid (Annelida, Polychaeta) from a Hydrocoral Off Central California. By William J. Light. Pp. 459–472. Vol. 37, No. 15: Benthic Fishes Cast Ashore by Giant Wales Near Point Joe, Montery County, California. By W. I. Follett. Pp. 473–488. (San Francisco: California Academy of Sciences, 1970.) [3112

Harvard University. Program on Technology and Society. Reprint No. 9: The Function of Tort Liability in Technology Assessment. By Milton Katz. Pp. 587–662. (Cambridge, Mass.: Harvard University, 1970.) [3112

Renin—Angiotensin Mechanisms—a Review of Research Grants Supported by the National Heart and Lung Institute, 1949 to 1970. By May Sherman. Pp. vi+140. (Bethesda, Md.: National Institutes of Health—Extramural Research and Training, 1970.) [3112

Bulletin of the American Museum of Natural History. Vol. 143, Article 3: Breeding Tubercles and Contact Organs in Fishes—Their Occurrence, Structure and Significance. By Martin L. Wiley and Bruce B. Collette. Pp. 143–216. (New York: American Museum of Natural History, 1970.) $2.25. [3112

International Union for Conservation of Nature and Natural Resources IUCN Eleventh Technical Meeting, New Delhi, India, 25–28 November 1969. (IUCN Publications, New Series No. 17.) Pp. 282. (Morges, Switzerland: IUCN, 1970.) [41

Studia Forestalia Suecica. Nr. 83: Mycorrhiza and Tree Nutrition in Poor Forest Soils. By Erik Björkman. Pp. 24. Nr. 84: Biological Control of *Fomes annosus* in Norway Spruce (*Picea abies*) with Immunizing Commensals. By J. L. Ricard. Pp. 50. 15 kr. Nr. 85: Low-Temperature Induced Irregularities in Pollen Mother Cells of *Larix leptolepis*. By Gösta Eriksson. Pp. 14. 5 kr. Nr. 86: Photo- and Thermoperiodic Responses of Different Larch Provenances (*Larix decidua* Mill.) By Milan Simak. Pp. 31. 9 kr. Nr. 87: Further Studies on Meiosis and Pollen Formation in *Larix*. By Gösta Eriksson, Inger Ekberg and Alena Jonsson. Pp. 65. 17 kr. Nr. 88: Plant Condition and Plant Growth—Planting Experiments with Spruce (*Picea abies* (L.) Karst.) on *Calluna* Heath Land. By Erik Björkman. Pp. 36. 9 kr. (Stockholm: Skogshögskolan, Royal College of Forestry, 1970.) [41

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US Department of the Interior: Geological Survey. Water-Supply Paper 1984: Hydrologic Effects of Floodwater-Retarding Structures on Garza-Little Elm Reservoir, Texas. By C. R. Gilbert and S. P. Sauer. Pp. vii+95+3 plates. (Washington, DC: Government Printing Office, 1970.) [61

Smithsonian Contributions to Zoology, No. 60: Studies of Neotropical Caddisflies. 10: Leucotrichia and Related Genera from North and Central America (Trichoptera: Hydroptilidae). By Oliver S. Flint, Jr. Pp. 64. (Washington, DC: Smithsonian Institution Press, 1970. For sale by US Government Printing Office.) $1.25. [61

Republic of South Africa. Department of Industries: Division of Sea Fisheries Investigational Reports. No. 84: Notes on an Oxygen-Depleted Subsurface Current Off the West Coast of South Africa. By A. H. B. De Decker. Pp. 24. No. 88: Marine Algae from Southern Africa. 1: Six New Species from the Inter- and Infra-Tidal Zones. By R. H. Simons. Pp. 13. (Sea Point, Cape Town: Division of Sea Fisheries, 1970.) [61

Fisheries Research Board of Canada. Technical Reports. No. 202: Utilisation des Diatomees Benthiques comme Indicateur de Pollutions Minieres dans le Bassin de la Miramichi N. W. Par W. K. Besch, M. Ricard et R. Contin. Pp. 72. No. 204: Tag Recaptures and Movements of Adult Male Snow Crabs *Chionoecetes opilio* (O. Fabricius) in the Gaspé Region of the Gulf of St. Lawrence. By J. Watson. Pp. 11. (St. Andrews, NB: Fisheries Research Board of Canada, Biological Station, 1970.) [61

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Cancer in Crisis. Pp. 72. (New York: Memorial Sloan-Kettering Cancer Center, 1970.) [81

US Department of the Interior: Geological Survey. Bulletin 1284: Paleozoic Stratigraphy in the Northwest Coastal Area of Prince of Wales Island, South-eastern Alaska. By G. C. Eberlein and Michael Churkin, Jr. Pp. iv+67+2 plates. $0.65. Bulletin 1294-B: Probable Permian Age of the Rampart Group, Central Alaska. By W. P. Brosgé, M. A. Lanphere, H. N. Reiser, and R. M. Chapman. Pp. iii+18. $0.20. Bulletin 1312-H; Geology, Mineral Deposits and Geochemical and Radiometric Anomalies, Serpentine Hot Springs Area, Seward Peninsula, Alaska. By C. L. Sainsbury, T. Hudson, R. Kachadoorian and Thomas Richards. Pp. iii+19+plate 1. Water-Supply Paper 1608-K: Water Resources and Related Geology of Dera Ismail Khan District, West Pakistan, with reference to the Availability of Ground Water for Development. By James W. Hood, Lutfe Ali Khan and K. Jawaid. Pp. viii+74+6 plates. Water-Supply Paper 1879-G: Dispersal of Plating Wastes and Sewage Contaminants on Ground Water and Surface Water, South Farmingdale-Massapequa Area, Nassau County, New York. By N. M. Perlmutter and Maxim Lieber. Pp. v+67+5 plates. Water-Supply Paper 1891: Geohydrology of Finney County, Southwestern Kansas. By Walter R. Meyer, Edwin D. Gutentag and David H. Lobmeyer. Pp. vii+117 +2 plates. (Washington, DC: Government Printing Office, 1970.) [111

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US Department of Agriculture: Agricultural Research Service. Miscellaneous Publication No. 1178: The Potential for Genetic Suppression of Insect Populations for their Adaptations to Climate. By W. Klassen, J. F. Creech and R. A. Bell. Pp. 77. (Washington, DC: Government Printing Office, 1970.) $0.60. [111

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Pollution in its Place

NATIONS are now accustomed to create committees for the study of pollution with all the zeal with which, in past decades, they have created national airlines, national broadcasting networks and the like, but Britain has been lucky in the most prestigious adventure of this kind—the Standing Royal Commission on Environmental Pollution with Sir Eric Ashby as chairman (see page 586). Although the commission's first report, now published, is more a prospectus for future work than a recipe for solving present problems, it has defined a sensible framework within which the analysis of environmental problems can be conducted in a levelheaded fashion. If only the document is widely read, the result could well be a better concentration of public and political interest on issues deserving of public attention. The difficulty is that the commission's advice, like that of all other royal commissions, can be religiously ignored by everybody concerned, even the government departments that helped to set it up.

The sobriety of the commission's view of the problem with which it has been saddled is well exemplified by what it has to say about the criteria on which decisions about the abatement of environmental nuisances should be based. The starting point for the discussion is a careful statement of the problem. The issue, the commission implies, is not so much how to abate pollution as of deciding how much to spend on abating pollution. Theoretical models are easy to construct, as any elementary textbook in economics will show. The commission says that the criterion for how much to spend is that pollution should be reduced to the point at which the costs are matched by the benefits. Presumably its intention is that in an ideally calculable world, the marginal costs and benefits should be equal. The immediate difficulty is that nobody has sure ways of calculating even the costs of reducing some particular forms of pollution to some predetermined level. Quantifying the benefits is, as the commission points out, necessarily a more chancy business, involving attempts to put a figure on the value of particular social assets. This is why the committee says—and everybody will applaud—that serious attempts should be made to define the economic quantities involved. But what will happen if nobody has the wit to provide an answer? One of the few parts of this first report at which the commission abandoned argument for arm-waving is that in which it draws an analogy between the way countries such as Britain have spent large sums on education without being able to put a figure to the benefits, and says that pollution and its abatement must similarly be dependent on value judgments. And if slavery has been abolished without the economic cost being held to be an obstacle to reform, is it not now sensible that society should "willingly incur expenditure on the protection of its own natural environment"?

Rhetorically, the question is unanswerable. In the years ahead, however, it is important that society should find ways of using in cost benefit equations factors which represent social benefits which are not easily quantified. To begin with, it is often the case that apparently imponderable benefits can be partially defined by means of upper or lower limits. In Britain, for example, it is by now well established that the death rate from bronchitis in north-west England is far greater than that south of the Thames and, even though climate and age distribution in the population may be concerned, so too is almost certain to be atmospheric pollution in the larger cities. After all, it is only a decade since old people in their hundreds were killed off in northern cities when sulphur dioxide and other noisome products were trapped beneath inversion layers. The Clean Air Acts notwithstanding, it is not improbable that air pollution as a cause of verifiable death continues in many parts of Britain. Here, then, is one means of providing a sombre lower limit to the number to be entered in the cost benefit equation. The fact that less tangible factors such as the possibility that there may be a link between air pollution of some kinds and lung cancer, for example, or the likelihood that clean air may enable people to be more cheerful cannot easily be cast in numerical form should be regarded not as a proof that the cost benefit equation is insoluble, but that there is a need for a better understanding of the factors not already quantifiable. The commission's use of the analogy of slavery and its abolition is in any case not all that convincing a proof that there must be circumstances in which important questions must be decided on stark ethical principles: apartheid in South Africa is an offence against decent values but also in an advancing society an economic handicap as well.

On the issue of which nuisances to deal with first, the commission also spells out the helpful principle that the management of the environment must be a deliberate process, with no crash programmes to distract attention from long-term goals. This is one of the most serious pitfalls in the planning of the environment. The temptation is to tackle first the problems that are easiest to solve. Where governments are concerned, it is also tempting first of all to deal with apparent nuisances which are cheap to abolish. This is much the spirit in which governments have sought to rid the environment of DDT and other persistent pesticides by imposing restrictions on manufacturers before anybody has had a chance to ensure that such a course will not entail an unwarrantable cost in crops or even lives destroyed by pests. By comparison, governments, even enthusiastic governments such as that in Washington, are comparatively slow to hand out public money for the abatement of public nuisances such as the practice in the United States of discharging large quantities of untreated sewage into rivers. If the Ashby commission's precept is to be taken seriously, the movement for a better environment will not merely be costed more precisely than in the past but will be given some sense of strategy to replace what has recently been a frenetic and over-zealous anxiety to do something that shows and which is quick. The commission does well to point out that the almost spectacular improvement of air pollution in Britain, a 50 per cent decrease of smoke pollution in a decade, has cost many millions of pounds spread over many years. This is not a field for fickle enthusiasts.

If the Ashby commission has left the economics of pollution for study by some other branch of government, it has also unfortunately skated over some of the legal issues to be decided. In the past several years, there has been a tendency to assume that only governments can act decisively in the abatement of public nuisances and, indeed, the spectacular developments of the recent past have all been represented by government decisions. But unfortunately, however, governments cannot always be relied upon to act decisively or even diligently, which implies that there is a need somehow to improve the institutions regulating the conditions of rivers, coasts and even the atmosphere. The ideal is that there should be self-correcting legal instruments or institutional arrangements which can help to make sure that those who use the environment in various ways are much more aware than at present of the potential cost of doing so. Where the pollution of rivers is concerned, for example, it would be only sensible if the statutory authorities called river boards which at present control some of the uses made of rivers were also given authority for the disposal of sewage in the corresponding catchment areas. This, as it happens, is one of the commission's specific recommendations in its first report and here, as luck will have it, there is a chance that the British government will do something effective. The general principle should be that opposing interests should as often as possible be fitted into the same framework of regulation and control.

However vigorous the war against pollution, however, nobody can be sure that the outcome will be a marked improvement in the quality of life as it is called. The trouble, of course, is that no amount of air cleansing equipment can make life in a badly planned city delightful. This is another of the general points made by the Ashby commission and one that should be taken seriously. If countries such as Britain are now determined to spend considerable sums on measures for the more effective control of pollution, they should also ask themselves whether the same result might not be achieved more simply and even more cheaply by more imaginative planning of cities and the countryside. Aircraft noise is the illustration that cries out for attention. Is it better that there should be research and development leading to less noisy but less efficient aircraft engines, or that there should be a sensible policy for the siting of airfields at places where the noise the aircraft make is immaterial? Similarly, in cities, a part at least of the traffic problem could be made to disappear if cities were planned in such a way that the need for physical movement was reduced or, alternatively, if orderly public transport were more attractive. This is a powerful reason why it will be a great misfortune if current concern about the environment, well intentioned and potentially beneficent as it is, turns out to be restricted simply to a campaign against pollution. Moreover, it is important to acknowledge that getting rid of pollution of any kind, like the building of more decently organized cities, is bound to be an expensive social investment. On the face of things, it looks very much as if the Ashby commission will turn out to be a powerful spur in this direction.

Teaching without Research

THE changing pattern of financial support for scientific research at universities was bound to have profound and lasting effects on the character of academic life and, in due course, on the character of university departments. The report of the Chemistry Committee of the Science Research Council (see page 587) is the latest sign of the way the wind is blowing. To begin with, the committee calculates that if there were be to a substantial increase in the annual output of PhD graduates there would be a problem in finding jobs for everybody. Luckily, it looks as if the annual output of PhD graduates will in fact be stabilized at less than 900, of whom 200 a year will find their way into teaching posts at British universities. The committee also draws attention to the need for some alternative method of allotting studentships to university departments so as to allow for the way in which a steadily growing number of university departments are anxious to take on the training of graduates and the academic research programmes which traditionally accompany this process. The solution, the committee suggests—and it is plainly flying a kite and not laying down policy—may be a more selective way of choosing the departments to which studentships will be allocated. Because in Britain the Science Research Council is a predominant source of stipends for potential PhD graduates, a process any more selective than at present used would be certain to have a powerful influence on the pattern of graduate training at the universities. What the committee is looking for is a formula for making sure that some would-be graduate schools will have no students to teach.

For the departments concerned, the consequences could be far-reaching, if only because the regular subvention of universities by the University Grants Committee is calculated after taking account of staff–student ratios which are more generous when the students are already graduates. A department denied studentships would quickly become a department in which research would have to be squeezed into a much more crowded teaching programme than at present and would be without the benefit of the interaction between teachers and graduate students. Will this not imply that in the comparatively near future, there will be a situation in which some university departments will be demonstrably different from others, more preoccupied with teaching and less with research? On the face of things, this would seem to be inevitable in the present situation in which the number of universities, or of university departments in particular disciplines, is too great for the amount of money available for research, but too little to satisfy the legitimate demands for undergraduate instruction. Moreover, it is important that even if the amount of money available for research were for practical purposes unlimited, the preservation of the genteel convention that all university departments can be graduate schools if they choose would create horrendous anomalies. In the sciences as a whole, roughly a third of all successful PhD candidates at present find their way into university teaching and the simple truth is that with present ratios of staff members to graduate students, a PhD graduate will more than replace himself during his career. In other words, either the amount of graduate training done by the university departments must be reduced or some ways must be conjured up for employing PhD graduates outside the universities—an unlikely prospect in present circumstances. The result seems unavoidable, and applies to departments other than chemistry departments—that in the future there is bound to be a modification of the old principle that all university teachers can be active research workers unless they decide otherwise. For one thing, there is not enough money. For another, the traditional assumption that research and the training of graduates must go hand in hand can only be implemented by training people for jobs that do not exist. It goes without saying that these tendencies will, if anything, be strengthened by the growing competence of the polytechnics in graduate training.

How should the universities respond? The first thing to say is that there is no special reason why universities should hang their heads in shame if some of them are forced by circumstances to concentrate on teaching. This, after all, is why they exist. In Britain, however, universities are unnecessarily fragmented by the tendency of the larger university departments towards fission. Every chemistry department, after all, is now at least a troika of inorganic, physical and organic chemistry. Biochemistry is usually something quite different. The result is that such research effort as there is must be scattered even more widely than is strictly necessary among a multiplicity of university departments and sub-departments. It is no wonder that many of these institutions are hard pressed to devise viable research programmes for themselves. Often, everything will rest on the shoulders of one energetic man with a clear idea of what he wants to do—and, by the same test, everything will collapse when he in his turn is snatched away to a more powerful appointment somewhere else. So is it not necessary, in the year ahead, that as a part of their adjustment to changing circumstances, university departments which have been traditionally split apart should be welded together in such a way that those academics whose energies will be principally concentrated on teaching should be enabled to rub shoulders and exchange ideas with people who are more actively engaged on research? Is it not also necessary to acknowledge that some university departments consecrated to subjects such as biochemistry and busily teaching undergraduates should be persuaded that their future also lies within a wider and more flexible framework? Biochemistry, after all, is hardly the kind of diet to be fed to undergraduates undiluted. In short, there is a need that universities in self-defence should do whatever they can to reorganize departments in such a way as to make them bigger, better coordinated and more capable of providing undergraduates with a variety of courses. The alternative is a more open and more immediate recognition that some university departments must be and will be treated less well than others in the same field.

There is also a need for some change in what is considered to be a proper activity for academics. In the years since the war, the convention has grown up that in the natural sciences, scholarship is represented principally by experimental research or some other activity absorbing most of every working day. Perhaps the time has come to ask whether this convention is essential. May there not even be advantages in a situation in which, as in the old days before the Second World War, research tended to occupy the months in the summer when the undergraduates were away? Then, at least, this scholarly activity would be something to look forward to. To be sure, in circumstances like these, it would be necessary to discard the convention that academic promotion is determined chiefly by production in academic research.

It goes without saying that the impending change, gradual though it will be, is certain to create tensions between the universities in which research will seem increasingly privileged or even a luxury and the research institutes elsewhere in which research is a full-time occupation. This is yet another reason for hoping that the inquiry into the pattern of British research now under way will look squarely in the face the problem of the intramural research carried out by the research councils, especially the Agricultural Research Council, the Medical Research Council and the Natural Environment Research Council. Nobody would expect there to be rapid changes in present arrangements and it is also important to devise some means of making sure that there remain ways in which some kinds of research of high quality can be carried on without the encumbrance of undergraduate teaching. In other words, there is a case for a much closer association between research institutes and universities—which is not in any sense to suggest that there are no close relationships at present. What this implies is that the coming pressure on resources for research will bring about a change not merely in the amount of research carried out in universities but in the quality of academic life as well. As things stand, the universities have it within their power to ensure that the qualitative change is not a deterioration.

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100 Years Ago

Sanitary Tests

DR. LANKESTER recently pointed out in NATURE that the existence and spread of fever were mainly owing to popular ignorance and the neglect of physiological laws. Since the article referred to was written, a greater plague has followed the fever then prevailing; and we are now told that Ireland is much better off than England—vaccination being there almost universal.

This state of things seems to me but a symptom of a more deeply-rooted evil, viz., the general neglect of physiological and sanitary science among the *higher* orders as well as the lower.

In how many large schools are the laws affecting the human body and the relation of man's frame to the destructive and constructive elements which surround us systematically taught? Are there any?

We talk of the gross ignorance and filthy habits of the poor; but both their ignorance and their filthiness are often a part of the very conditions of their existence. Have *we* been faithful stewards in this great matter?

Allow me to draw attention to the fact that, though Government has greatly facilitated and cheapened the acquisition of other branches of science, hygiene seems entirely omitted from the programme. But knowledge must descend from the higher to the lower levels. Ought not the heads of all public schools to undergo a compulsory examination in this subject? I could adduce instances where the greatest mischief has resulted from ignorance in such high quarters.

Aigburth, Liverpool, Feb. 25 SAMUEL BARBER

From Nature, 3, 347, *March* 2, 1871.

OLD WORLD

Royal Commission Provides Framework for Study

ANOTHER report on pollution has been placed on the already overloaded desk of Mr Peter Walker, the Secretary of State for the Environment. Although the report has few concrete recommendations to make, Mr Walker would do well to study its contents very carefully. It is the first offering from the Royal Commission on pollution (HMSO, 45p), set up last year under the chairmanship of Sir Eric Ashby, and it comes up with the uncontroversial conclusion that although there has been considerable improvement in some aspects of Britain's environment, there is little room for complacency. But the chief value of the report lies in its analysis of the problems caused by pollution and in its review of the present state of Britain's environment.

The report in many ways prepares the ground for further investigation by the commission, and to this end there is an analysis of the pollution problem in terms of the costs and benefits of its abatement. Much of the analysis is old hat—the commission points out, for example, that one of the chief reasons for pollution is that the costs which it involves are not usually borne by the polluter, and there is thus insufficient incentive for pollution control. But the point that there is need for an economic framework for a full cost/benefit analysis of pollution control is made by the commission with considerable conviction. It also takes pains to point out that "the social benefits of cleaner air and water, less noise and a more pleasant landscape, have to be put into perspective with other claims on resources, such as housing, health and education".

As far as the present state of the environment is concerned, the commission has a few comforting things to say about air pollution, especially the effects of the Clean Air Act in the south of England, but it is rather more gloomy about other forms of pollution. As a result of smoke control, the winter sunshine in London has increased by 50 per cent since 1950, and in spite of an increase of 17 per cent in gross energy consumption, the emission of smoke and sulphur dioxide into the atmosphere has decreased dramatically (see Fig. 1). But conditions in some of the towns in the north of England are much less pleasant, and there, the commission says, "there is urgent need for more vigorous application of the Clean Air Act". Pollution from road vehicles is also a cause for concern, chiefly because there is insufficient knowledge about the effects of long term exposure to various components of exhaust fumes, and the commission warns that "it would be dangerously complacent to ignore" the projected increase in the volume of road traffic in Britain.

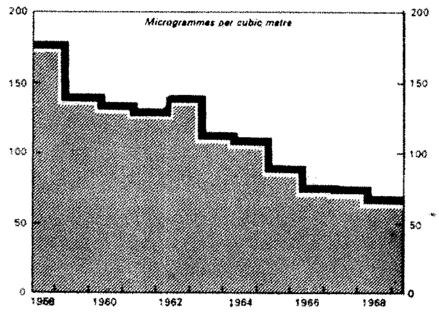


Fig. 1 Average smoke concentration near ground level in the UK, 1958–1968.

Turning to pollution of the land, Sir Eric Ashby's commission casts a glance at the United States, finds that the average amount of domestic refuse produced per person each day is nearly twice that in Britain and warns that Britain is likely to face a mounting refuse disposal problem. Already, 14 million tons are dumped on areas of unused land, and the only solution the commission has to offer is that salvage and recycling techniques must be improved. As for pesticides and fertilizers, the drive for less persistent fertilizers should be speeded up, and "valuable manure from intensive farming is being wasted", and consequently there is a growing risk of soil deterioration.

But it is in the area of marine and freshwater pollution that the commission sees most cause for concern. Although 73 per cent of Britain's rivers are classified as unpolluted, 12 per cent are either "grossly polluted" or "urgently needing attention". Pollution from phosphate fertilizers, which run off the land and lead to outbursts of aquatic plants in rivers and lakes, is not yet a grave problem but it is one which cannot be glossed over, the commission suggests, and an even higher standard of effluent purity must be achieved if the demand for domestic water is to be met. While there is cause for concern about river pollution, however, there is even more to worry about in the sea. Along the east and south coasts of England alone, for example, 5 million cubic metres of domestic waste, 3 million cubic metres of industrial waste and 7 million cubic metres of power station cooling water are dumped into the sea every day, and the commission says that "the estuaries and inshore seas are increasingly treated as an open drain and dumping ground". Surprisingly, there is no evidence of widespread damage to marine life in British waters, but there is an obvious need for more research on the effects of pollution on the life of shallow seas. The situation is so serious in the eyes of the commission that it has decided to make pollution of tidal waters, estuaries and seas around Britain's coasts its chief topic of study this year.

Disposal of radioactive waste also came under the commission's scrutiny, and no immediate cause for disquiet was found. There is, however, a need to bear in mind the problems that are going to accrue from increased use of nuclear energy, and the commission suggests that, although arrangements for the disposal of radioactive material should lie in the province of international control, the problem needs foresight.

The commission also has a few things to say about some of the popular horror stories about global effects of pollutants. The so-called greenhouse effect, for example, in which the increasing amount of carbon dioxide in the atmosphere (see Fig. 2), acting as a type of window, lets visible radiation pass through but filters out some of the long wave radiation from the Earth, has often been singled out by popular writers for dishonourable mention. The theory is that the heating up of the atmosphere which would result from this process would melt the polar ice caps, and wreak untold damage on low-lying coastal areas, but the commission says that the available evidence is not strong enough to support such a theory. More research needs to be carried out on the exchange of carbon between the oceans, plants and the atmosphere before such a theory can be proved or discredited. Nevertheless, the evidence available so far points to the possibility of an increase in

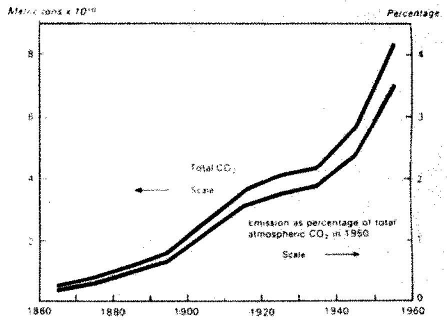


Fig. 2 Carbon dioxide from the combustion of fuels in the world, 1860–1959.

atmospheric temperature of only 0.1 to 0.2° C, and this is unlikely to be significant.

The commission comes to similar conclusions about the effects of water vapour and trace amounts of pollutants in the stratosphere—a topic which has caused considerable speculation, especially from opponents of the supersonic transporter. There is therefore "no cause for alarm" about the global effects of pollution, but the commission recommends "the extension of international monitoring of the atmosphere and the maintenance and extension of fundamental research on an international basis on the natural chemical and physical processes, both within the atmosphere and between the atmosphere and the surface of the planet".

CERN

Green Light for 300 GeV

After nearly four years of indecision and changing of plans, the CERN council has at last given the official go-ahead for the 300 GeV proton synchrotron to be built at Geneva. Ironically, the indecision and early disputes about the possible site for the accelerator have produced a relatively cheap and very flexible proposal which arose last year like a phoenix from the ashes of earlier plans. When the CERN council met last week to carry on the meeting that was adjourned last December, ten out of the twelve member states pledged their support for the plans and only two delegations—those from Greece and Denmark—had to declare their governments' unwillingness to take part. This means that the cost of the project—estimated to be about £90 million over a period of eight years—will be divided chiefly between West Germany who will contribute 24 per cent, Britain (22.5 per cent), France (20.5 per cent) and Italy (13.3 per cent).

The council meeting was adjourned last December when it became evident that the governments of some of the smaller countries needed more time in which to make up their minds about the proposals. But agreement was also prevented because the British delegation, led by Sir Brian Flowers, was hamstrung by the condition imposed by the government that British support would only be forthcoming if the council decision were unanimous. Happily, this condition was relaxed and the British delegation was not placed in the unenviable position of watching the whole project paralysed by the abstention of Denmark and Greece.

The Greek delegation said that although it believes that the 300 GeV project is very worthwhile, the Greek government has no money to spend on it, while the Danish delegation said that a final decision on participation in the project must await the findings of a review of Denmark's policies for international cooperation in science. As for participation by Norway and Sweden, these countries are prepared to back plans which entail an expenditure no greater than the 1,124 million Swiss francs that was first envisaged when the new proposals were drawn up last April.

The machine will be built underneath the Switzerland/France border next to the site of the present CERN 28 GeV proton synchrotron, which will be used to feed protons into the accelerator. The accelerator tunnel itself will be 2.2 km in diameter, bored through rock, and it will be essentially the same project that was first mooted last April by Dr John Adams, the director of the project. The beauty of the plan is that it removes at one blow the bitter disputes about where to site the machine and it also allows much greater flexibility in design. But by far its most powerful trump card is that it is about one third cheaper than the original design.

The idea is that the machine would first be built to a capacity of 150 GeV by using only half of the proposed magnets for bending the proton beam. The remaining magnets will therefore be installed at a time when it should be possible to assess the viability of superconducting magnets, and three choices will be open to the planners. The remaining magnets could either be of a conventional design, to give a machine of 300 GeV capacity, or they could be superconducting, to give a 400 GeV machine. Alternatively, if the original magnets were also replaced by superconducting magnets, the capacity of the machine may be as high as 800 GeV. The crucial decisions on magnet design will have to be made early in 1974, by which time the 150 GeV machine should be ready for operation. If it is decided to go straight to the 300 GeV machine using conventional magnet technology, this could be completed by the end of 1976.

This flexibility in design would have been lost if the original plans for the machine were adopted. The accelerator would also not have been linked to the 28 GeV facility in Geneva, and there was considerable dispute among the member countries about the ideal site for the project. The disagreement about the siting of the machine was sharpened by the high costs of the project—about 1,900 SF—and in 1968 the British government decided, against the advice of the Council for Scientific Policy, that it wanted no part in the project. This decision caused considerable heart-searching among the other member countries, and a cheaper, less satisfactory and watered down version was proposed. Agreement was, however, not obtained for this proposal, and the present plans were put forward just as it seemed that the project was unlikely ever to get off the ground.

The decision to go ahead with the accelerator will have major implications for high energy physics in Europe (see page 594), but it will certainly not leave the domestic programme for elementary particle physics in Britain entirely unscathed. The British contribution to the project will work out at an average of about £3 million a year for the next eight years and this will be taken from the budget of the Nuclear Physics Board of the Science Research Council. The board pointed out in the annual report of the Science Research Council that "the sacrifices that must be envisaged to achieve the 300 GeV objective have sharpened", but since then the proposed budgets of the research councils have been cut by the government, and the effects of entry to the project are likely to be even more keenly felt.

One consequence is that the Nuclear Physics Board has not sought funds for any major domestic facility over the past few years, and the growth in academic manpower has been held in check. If there is any more slimming to be done in elementary particle physics in Britain, the SRC is being coy about where the cuts are to be made. It seems, in any case, that there is little likelihood that the number of British particle physicists will be increased, and the scientists at the Rutherford high energy laboratory and at the Daresbury electron facility will be able to breathe more easily when the SRC makes known its thinking about domestic high energy physics.

CHEMISTRY

Policies for Change

A halt in the rate of growth of research studentships in chemistry and more flexible postgraduate studies are likely to be the chief changes in the policy of the Chemistry Committee of the Science Research Council in the next few years. This means that after a sharp increase—35 per cent between 1967 and 1969—the total output of PhD graduates from chemistry departments in Britain will remain static at just over 850 a year for several years. But even this strong pressure on the brake will not alter the situation in which more PhDs are being produced than are needed for research and teaching, and the chemistry committee of the SRC will therefore view broader and more flexible courses of study with some favour when it shares out its funds for student support. This indication of the SRC's policies for postgraduate education is contained in a review carried out by the chemistry committee (*Chemistry—a review of the policies and activities of the Chemistry Committee of the Science Research Council*, available free from the SRC), and the committee is no less explicit in its statements of policy for supporting research in chemistry.

Sticking closely to the policy of selectivity as outlined in the annual report of the SRC for 1969–70, the chemistry committee has been devoting some 20 per cent of its £1.5 million for research to selected areas, and distributing the remainder to "any spontaneous proposal judged to be of high scientific merit". Chief beneficiaries of this policy of selectivity have been polymer science and enzyme technology, and the committee has recently invited applications for research support in organometallic chemistry and photochemistry. Possible economic benefits are obviously at the back of the committee's mind when it designates areas for selective support but, although the committee pays lip service to the concept of innovation in the chemical industry, there is little evidence in the report that the committee seeks out and supports research of an unashamedly commercial nature.

As for future patterns of selective support, the committee singles out colloid chemistry as a likely candidate and has set up a panel to survey the subject. Nevertheless, "at this stage it is by no means clear that the committee will decide to give selective support to this subject", the committee warns. Whatever the panel's verdict, the committee says that it requires more information on the success of its support of photochemistry and organometallic chemistry before venturing into similar policies and, in any case, no more than one fifth of its funds should be devoted to selected areas.

While there are few major changes in the offing in the pattern of support for research, support of postgraduate training in chemistry seems unlikely to remain unchanged. As far as the SRC is concerned, the emphasis is now going to be on more flexible courses. The committee has calculated that there will be no substantial increase in the number of chemistry graduates at first degree level in the next few years, and, if present policies are not changed, that the growth in the output of PhD chemists is also about to flatten off at about 860 a year. The SRC supplies the largest source of support for postgraduate studies in chemistry (about 530 a year), and the chemistry committee suggests that the total number of SRC research studentships available to chemistry departments should not be substantially changed in the next few years.

To support this policy, the chemistry committee has carried out a brief survey of the job market for postgraduate chemists and it comes up with the finding that there will be about 870 jobs a year available for PhD chemists, assuming that about 120 immediately go abroad. But the committee is quick to point out that only about 700 of these jobs require a strongly research-oriented education in chemistry, and there is therefore some room in the system for experimenting with more flexible courses. To be sure, the SRC has already made some changes in its awards policies—in 1967 the Cooperative Awards in Pure Science scheme was introduced and in 1969 90 SRC studentships in chemistry out of a total of 514 were awarded to industrially linked projects under this scheme. The committee is now, however, casting an approving eye on the Swann-type PhD courses with a strong core of research training and further study in other areas, and it puts the ball firmly in the universities' court by saying that it wishes "to encourage departments to propose new schemes along these lines, to provide a broader training both for the convinced researcher and for the man whose subsequent career is not likely to be concerned with research".

The chemistry committee also believes that there should be provision in the award of studentships for postgraduate students to change their course of study. The problem at present is that students accepted for PhD courses have little chance to change their studies because they would be likely to lose their grant. The universities themselves are also unwilling to admit that a wrong choice was made if a postgraduate student does not reach the standard expected of him. The answer, the chemistry committee suggests, may be to allow students to spend the remainder of their award on some other form of training, for example a diploma in management studies. Under such a scheme, a postgraduate student would be able to end up with two different qualifications—an MSc and a diploma. This scheme is at present being looked at by the committee and it seems likely that it will be met with approval.

The publication of this review of the policies of the chemistry committee is a welcome step away from the obsessive secrecy that has characterized much of the workings of the research councils in the past. It is certainly tangible evidence that the SRC intends to take seriously its intention not to hold its cards quite so closely to its chest, and other research councils would do well to follow suit.

COMPUTER POLICY

Software Firms Boosted

IMPORTANT changes in government policy toward the computer industry were revealed last week. Representatives of the Civil Service Department (CSD) told a subcommittee of the Select Committee on Science and Technology that the role of their department is shifting, and a new attitude to the software industry, which marks a significant change from that during the Labour government, is emerging. At the same time the CSD's representatives, ably led by Mr A. A. Creamer,

Table 1 Computers in Use in Government Departments at December 31, 1970
Number and series of computers used by departments, the hardware cost and specialist staff employed

Department	Number of computers	Number of computer series	Cost (£'000)	Systems analysts and programmers (March 1970)
Agriculture, Fisheries and Food	4	3	1,189	66
Aviation Supply	28	11	2,982	67
Central Statistical Office	1	1	48	6
Customs and Excise	1	1	317	67
Defence (Navy)*	48	17	4,254	973
(Army)	25	7	3,906	
(Air)*	29	8	4,321	
(Central)*	14	5	2,502	
Education and Science	2	2	361	61
Employment	2	2	708	85
Environment	13	6	1,998	207
Export Credit Guarantee Department	1	1	64	6
Foreign and Commonwealth Office	2	1	59	10
Health and Social Security	11	4	4,619	335
Home Office/Metropolitan Police	4	3	626	111
Inland Revenue	5	3	869	152
National Savings	3	1	1,779	104
Office of Population Censuses and Surveys	2	2	382	69
Ordnance Survey	1	1	94	12
Paymaster General	1	1	460	22
HM Stationery Office	4	3	1,142	89
Trade and Industry	25	14	5,351	162
HM Treasury	1	1	176	—
Scottish Office	6	4	618	75
Two departments without installations	—	—	—	30
Total	233		38,805	2,709

* Including some used for flight and training simulation.

gave the latest figures for the numbers of computers and associated staff in government departments (Table 1). But the subcommittee, and the civil service witnesses who have been appearing before it, are obviously hamstrung by having to wait for Mr John Davies or one of his colleagues to come down from the mountain with the promised ministerial statement on the support for the British computer industry.

The CSD has taken to heart comments made before the Select Committee last year that the government was relying too much on its own internal programming resources in its assessment of government use of software. The witnesses revealed that the volume of business placed with outside software houses will now rise from £570,000 in 1969/70 to more than £1 million in 1970/71 and possibly to more than £1.5 million in 1971/72. But, like the other witnesses who have appeared this year, the CSD thought it would be even harder to distinguish between British and foreign software for the purposes of giving preference than it is to say which computers can be called British. Mr Creamer also said that ICL has less software available than American companies, but what they have is good and fulfils the government's requirements.

Apart from doctrinaire reasons, it looks as if one of the explanations for this significant shift in policy which will delight the software houses is that the government is having difficulties in training and keeping systems and programming staff.

As things stand, however, ICL continues to be the apple of the British government's eye in the hardware field. The CSD witnesses revealed that in the year ending on March 31, they expect 50 per cent of large computers and 86 per cent of small computers for the government to be bought through single tender contracts, and ICL will be the beneficiary with the exception of one or two small orders to Honeywell and IBM. In the same period up to March 31, the government will place £18,189,000 worth of orders for administrative and general purpose computers, of which £16,543,000 worth will be bought from ICL. But it seems that the government has no intention of boosting ICL further by ordering computers in bulk. Last year the managing director of ICL told the Select Committee that his company had never been asked for more than four of a particular type of computer at once, whereas the United States government sometimes purchases computers in large batches to the benefit of American companies. According to the CSD witnesses, however, the British government has not been offered a good enough discount to balance the disadvantages of bulk ordering.

Since last year when the CSD defined itself as the central coordinator which ensures that government policy on the use of computers within departments is correctly applied, there seems to have been a devolution of responsibility to the departments themselves. Instead of providing detailed support to the departments, CSD staff are being redeployed "to a more active role of planning, proposal of common policies and promotion of technical developments of common interest". This has been made possible by the growing competence of the departments. In cases where departments still need help the practice now will be to call in the computer service industry.

Sakharov's Rights

from our Soviet Correspondent

Dr Andrei Sakharov, the Russian physicist and campaigner for human rights, has been told by the Procurator General of the USSR, Roman Rudenko, that he must either disband his unofficial "Committee for Human Rights" or else register it with the state. Dr Sakharov, well known already for his appeals of June 1968 and April 1970 for greater academic and personal freedom, founded his committee last November. The original members were Dr Sakharov himself, Valerii Chalidze and Andrei Tverdokhlebov. From the beginning, the committee stated that it would have nothing to do with any foreign or domestic organizations that were anti-Soviet.

According to Soviet law, any organization, whatever its aims and activities, must be registered. When founding the committee, Dr Sakharov announced his willingness to comply with this regulation. It seems, however, that for three months the official attitude to the committee has been ambivalent—whether to approve it and thus tacitly to admit the need of such an organization, or to ban it and thus give evidence of such a need.

The new move by Procurator-General Rudenko seems designed to bring matters to a head. Official recognition is hardly to be expected, yet it is difficult to imagine Dr Sakharov either abandoning his human rights campaign or discrediting himself by putting himself outside the law. So far, his appeals have always been based on the proposition that greater personal and academic freedom can only be to the benefit of the Soviet Union; his dissent, he maintains, is motivated by loyalty to his country. It would be ironic, indeed, if that very loyalty should now put him outside his country's laws.

Parliament in Britain

NRDC

Mr John Davies, Secretary of State for Trade and Industry, said that a review is being carried out of the arrangements for the exploitation of inventions resulting from public research and the support by the National Research Development Corporation for the development and exploitation of inventions from other sources. This review is being undertaken by Mr Docksey, formerly general manager of the research and technical development department of British Petroleum Ltd, and it should be completed well before the end of this year. (Written answers, February 17.)

Pollution and Sewage Disposal

The government intends soon to announce its conclusions on the chief recommendations of the Working Party on Sewage Disposal. Announcing this, Mr Peter Walker, Secretary of State for the Environment, said that the proposal for combining water authorities with sewage authorities has been considered by the Central Advisory Water Committee, and this body has recently completed a report of its findings.

Asked by Mrs Kellett about the progress of his review of the effects of all forms of pollution, Mr Walker said that he is reviewing the whole question of pollution of rivers and seas. (Written answers, February 17.)

Students' Grants

Mr William Van Straubenzee, Under Secretary, Department of Education and Science, said in reply to a question from Mr Kenneth Marks that it would cost £35–40 million in the current academic year to abolish the parents' contribution to grants for students in higher education. Mr Marks also asked the Secretary of State for Education and Science whether she will introduce legislation to extend mandatory grants to students on full-time Higher National Diploma courses, and also whether she will set up a working party to examine the question of parental contribution to student grants. Mrs Margaret Thatcher promised that both these questions will be considered during the current review of grants. (Written answers, February 22.)

CS

Mr Richard Sharples, Under Secretary at the Home Office, said that the committee under the chairmanship of Sir Harold Himsworth which is looking into the effects of the use of CS in Northern Ireland will not now be reporting until about the middle of this year. It was originally hoped that the committee would have reported last autumn, but it is still taking evidence. (Written answers, February 18.)

NEW WORLD

Nixon and Kennedy peddle Rival Cancer Cures

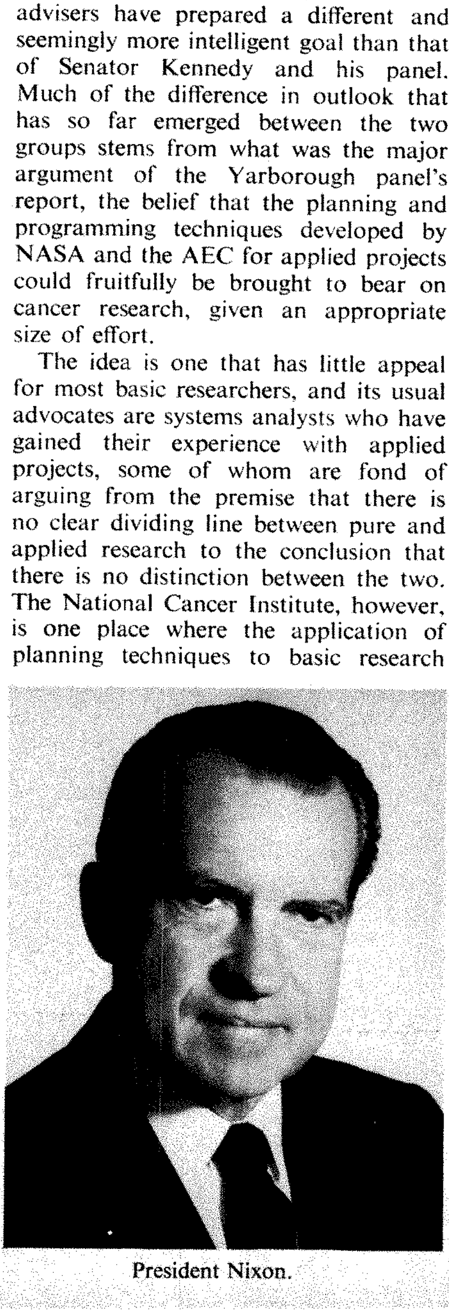
by our Washington Correspondent

THE proposal to infuse additional hundreds of millions of dollars into cancer research has become the subject of political rivalry between President Nixon and Democratic Congressmen led by Senator Edward M. Kennedy. Cancer researchers, interested only in seeing which group will outbid the other, are encouraging the contest with virtual assurances that a cure for cancer can indeed be bought if only the investment is sufficiently substantial. Beneficiaries of the new largesse—Congress, it seems, will be concerned to debate only its size—will include cancer research centres certainly, the wider field of biomedical research probably and cancer sufferers possibly, since nobody can be sure that the new funds may not perhaps hasten by a brief interval the cures for some kinds of cancer.

The proposal surfaced last December with the report of a panel of consultants commissioned by Senator Ralph Yarborough which advocated the setting up of a national cancer agency, separate from the National Institutes of Health, and funded at the level of $1,000 million a year. The proposal was adopted in outline by President Nixon in his budget message last month, in which he earmarked a fund of $100 million for cancer research in addition to the $230 million budget of the National Cancer Institute for the financial year starting this July (see *Nature*, **229**, 292; 1971). In his health message to Congress last week, Mr Nixon made slightly clearer his plans for the disposal of these funds; rejecting the idea of a separate agency, the President said a Cancer Conquest Program would be set up in the office of the Director of the National Institutes of Health. The Program will have a director (yet to be named) and a new Advisory Committee on the Conquest of Cancer, but the precise relation between these and the director of the National Cancer Institute with its National Advisory Cancer Council remains obscure. Meanwhile Senator Kennedy, who has succeeded the defeated Yarborough as chairman of the Senate's health subcommittee, introduced on January 26 a resolution calling for implementation of the consultants' panel proposal, though with an anticipated maximum budget of $600 million a year, compared with the $1,000 million income advocated by the panel. Chiding the President for the attempt to steal his clothing, Kennedy remarked in introducing the bill that "Now that President Nixon has joined us in our commitment to the goal (of conquering cancer), I am hopeful that Congress and the Administration will act rapidly to complete the action that has been so well begun."

Although Mr Nixon has certainly joined the cancer crusade, he and his advisers have prepared a different and seemingly more intelligent goal than that of Senator Kennedy and his panel. Much of the difference in outlook that has so far emerged between the two groups stems from what was the major argument of the Yarborough panel's report, the belief that the planning and programming techniques developed by NASA and the AEC for applied projects could fruitfully be brought to bear on cancer research, given an appropriate size of effort.

The idea is one that has little appeal for most basic researchers, and its usual advocates are systems analysts who have gained their experience with applied projects, some of whom are fond of arguing from the premise that there is no clear dividing line between pure and applied research to the conclusion that there is no distinction between the two. The National Cancer Institute, however, is one place where the application of planning techniques to basic research has a firm intellectual foothold, and it may be that the Yarborough panel of consultants gained some of their ideas from this source.


President Nixon.

The analogy of conquering cancer by the same methods used to get to the Moon is at any rate one that is easy to sell to politicians. "The time has come," Mr Nixon said in his State of the Union address last month, "when the same kind of concentrated effort that split the atom and took man to the Moon should be turned toward conquering this dread disease". The same words were mouthed by Senator Kennedy in introducing his Conquest of Cancer bill: "The bill I am proposing will establish an independent agency . . . modelled along the lines of NASA which succeeded so brilliantly in reaching our goal of landing a man on the Moon in the decade of the sixties." And Congressman Cornelius E. Gallagher, introducing a similar bill into the House of Representatives on January 22, asked for the "piddling sum" of $650 million a year for the next ten years (at the end of which, presumably, cancer would be vanquished) to be "controlled and directed by a National Cancer Authority which would have the same absolute direction of the cure and control of cancer that the National Aeronautics and Space Administration had over our conquest of space". The recent intellectual history of cancer research in Congress would not be complete without mention of the resolution introduced by Congressman John J. Rooney and passed by the House without dissent, that the conquest of cancer should be completed by 1976.

While Congressmen have remained content to regard the cure of cancer as a problem equivalent to the Apollo project, a thesis of which cancer researchers have done the minimum to disabuse them, President Nixon has of late been better advised. In his health message he explicitly denied the man-on-the-Moon theory of cancer he had promulgated in the State of the Union speech less than a month earlier. In the space programme, Mr Nixon remarked last week, "the challenge was technological; it did not require new breakthroughs. Unfortunately this is not the case in biomedical research at the present time; scientific breakthroughs are still required and they often cannot be forced, no matter how much time and money is expended".

Senator Kennedy.

Having repudiated the Apollo analogy, the President went on to justify the new cancer initiative by his belief that new breakthroughs in cancer are imminent:

A possible reason for this shift of emphasis may have been the soundings taken by the Office of Science and Technology, which would presumably have sensed a certain antipathy among the scientific community towards the man-on-the-Moon theory of cancer. At any rate, to herald the Administration's abandonment of this idea, the President's Science Adviser was dispatched to Chicago a week before the President's health message. In the course of a speech to the Association of American Medical Colleges, Dr Edward E. David explained not once but on four separate occasions that what the President had really meant in saying conquering cancer was like getting to the Moon was in fact that the two goals differed considerably. ("The President clearly recognizes the subtleties behind this statement" was the way David put it.) The nature of cancer research, David said, "presents a stark aspect with Apollo and nuclear energy. Indeed we do not believe in an AEC or NASA for cancer".

David's speech constitutes an important reinterpretation of the Administration's attitude not only on cancer research but also towards the biomedical community at large, for whom David had some highly conciliatory remarks. It would be wrong to set up a separate cancer agency outside the National Institutes of Health (another major difference between the Nixon and Kennedy proposals) because, David argued, the cancer problem straddles virtually all the life sciences and hence, he implied, all should benefit accordingly from infusion of funds. "The President is also aware that this new venture must not be undertaken at the expense of the broad base of scientific research. We must maintain the vigour, diversity and sparkle of biomedical research".

David also went out of his way to recognize the concern of the biomedical community about the fellowships and training grants administered by the National Institutes of Health. Although these are budgeted to remain constant next year, they reportedly escaped the knife of budget pruners only by a narrow margin. The President does not take a dogmatic stance about these grants and is waiting for the completion of an NIH study before deciding what arrangements to make for the support of students and trainees in the life sciences. "We welcome your voice in the debate over this issue," the Science Adviser told his Chicago audience, promising that "we will not move precipitously or capriciously but we need courageous assessments on your part. By courageous, I mean assessments which can lead to change where it suits national objectives".

David's address has been well received in the scientific community, in which he seems to have won wide support for Mr Nixon's initiative both outside and within the ranks of cancer researchers. "David's remarks were pretty sensible," was the reaction of one biologist last week. "I thought David's speech was splendid," said Professor Sol Spiegelman, director of the Columbia University Institute of Cancer Research. "A lot of us were against setting up a separate cancer agency divorced from the life sciences—David put it as well as a lot of scientists would".

Members of David's office are concerned to stress that they found a consensus of opinion among life scientists that this is a propitious moment for launching a new effort on cancer. Another factor behind the office's support of the proposal seems to be the feeling that this is a test project to see how well basic research can be harnessed to the problems of society, because cancer encompasses so much of modern biology the new effort cannot help having wide ramifications throughout the life sciences, but the Office of Science and Technology does not seem to have given attention to the specific aspects of research that justify the proposed new investment, regarding this as a matter to be decided by the scientists directly involved.

Dr Robert Q. Marston, director of the National Institutes of Health, said last week that while he had "no intention of using these funds other than as the President has indicated—to focus on cancer research—there are many areas of biological research directly related to the cancer programme".

Obvious research fields in which to concentrate the new support include viral oncology, cancer chemotherapy, chemical carcinogenesis and immunology. The extra funds will allow the National Cancer Institute to fund a larger portion of its research applications (last year only half the applications were approved, and of these 40 per cent of continuing projects and 10 per cent of new applications were funded). But Marston said the President's instructions were for the NIH to support not only individuals but also the more highly directed cancer programmes, to which the National Cancer Institute already devotes 40 per cent of its funds. "Both the President and the Yarborough panel recommended that we utilize modern management techniques in the cancer programme".

The Yarborough panel was in fact doing scarcely more than tell the NCI to do more of what it does already, since under the leadership of its director, Dr Carl G. Baker, the institute has probably acquired more experience in applying modern management techniques to research than any other members of the NIH. Formerly the chief of the NCI's programme planning section, Baker, on becoming acting director of the NCI, appointed to his old job a non-scientist with experience in managerial and planning techniques, Mr Louis M. Carrese. Formerly vice-president for management with the Frederick Research Company, an organization specializing in military systems and analysis, Carrese turned down offers from NASA and the Department of Defense to join the NCI in 1962.

Carrese believes the most fruitful opportunity for planning cancer research lies in the borderland between basic and applied research. Research, he says, should be defined in terms of specific objectives, such as particular human cancer problems, not conducted on an open ended basis. With Baker as co-author, Carrese has said (*Management Science*, **13**, B-420, 1967) "a project judged to be excellent from a scientific frame-of-reference does not necessarily mean that it is of strategic significance from the programme standpoint".

Two of the programmes designed on the basis of this approach are the Special Virus Leukemia Program, now the Special Virus Cancer Program, and the Cancer Chemotherapy Program. A notable success of Carrese's methods is the recent demonstration by the former programme that none of the 31 adenoviruses cause cancer in man, an important result attained in only nine months' work. The Cancer Chemotherapy Program also has its successes, having discovered and taken through to the clinical evaluation stage nine new chemotherapeutic agents of use against various kinds of cancer and evaluated 30 others. These drugs have certainly helped to prolong the lives of many cancer patients, but apart from the special cases of Burkitt's lymphoma and choriocarcinoma, cancers which are uniquely susceptible to chemical agents, the programme has not brought a cure for cancer any nearer, despite the $330 million that it has absorbed since it began in 1955.

Outside the immediate field of cancer research, there is apprehension that too large a proportion of the additional funds in the offing may be devoted to plannable research and too little to basic research which alone can afford a fundamental solution to the cancer problem. "At a certain level the new initiative is a disaster," one eminent biologist said last week, "since three-quarters of the relevant work for cancer is not being done in the name of cancer research. I think the people at the NCI will have to use their heads not to pilfer it all away. If they spend $50 million on searching for a virus in breast cancer, or providing electron microscopes in Nebraska, or funding research in cancer centres as a form of psychiatric care for doctors to give them the impression of doing research, then they're going to get nothing for their money."

This gloomy view of the hard road ahead is not shared inside the National Cancer Institute, and indeed Baker, in testimony before the House Appropriations Committee on April 23 last year, stated, "there are many scientifically based reasons for believing that not all but most cancer might be preventable if we are willing to make the investment". This view is subscribed to by other cancer researchers, more than 600 of whom endorsed the resolution introduced last month into the House of Representatives by Congressman Gallagher, calling for a NASA-type conquest of cancer. The 600 cancer researchers subscribed in particular to this statement: "We further express our conviction that with the level of funding and the magnitude of commitment authorized under the Gallagher resolution, cancer can be cured and controlled." It is little wonder that outside the ranks of cancer researchers there are fears of a backlash against all kinds of science from a public conditioned to believe by both politicians and scientists alike that a cancer cure is as attainable as the Moon.

Udall Praises NAS

by our Washington Correspondent

THERE was praise from an unexpected quarter for the National Academy of Sciences at the hearing held last week by the Department of the Interior on the proposed construction of an oil pipeline across Alaska. Stewart L. Udall, former Secretary of the Interior under the Kennedy and Johnson administrations, criticized the department's recent report recommending in favour of the pipeline and blamed it for having failed to seek advice on the matter from such "superior outside consultants" as the National Academy of Sciences.

Udall, who is head of an environmental consulting agency, known as the Overview Group, last referred to the academy in a speech delivered to the AAAS meeting in Chicago last December. On that occasion he assailed the academy for having failed to speak out earlier and move vociferously in defence of the environment, calling it a puppet of government that only gave the answers it was asked for. These remarks provoked a sharp response from the president of the academy, Dr Philip Handler, who countered that Udall had wholly ignored the academy and its reports on the environment during his secretaryship; "Udall seems to have discovered the environment after he left his post as Secretary of the Interior," Handler said (*Nature*, **229**, 151; 1971). Now, it seems, Udall has discovered the academy in a fresh light; his Alaska hearing speech sounds quite close to an apology.

Salaries of US Scientists in 1970

Scientific and Technical Field	Lower decile	Lower quartile	Median	Upper quartile	Upper decile
All fields (in dollars)	9,500	11,900	15,000	19,100	24,500
Chemistry	9,600	12,000	15,300	19,200	24,000
Earth and Marine Sciences	10,000	12,000	14,900	18,400	23,100
Atmospheric and Space Sciences	10,000	12,700	15,200	18,400	22,300
Physics	10,000	12,000	15,900	20,000	25,000
Mathematics	9,000	11,000	14,300	19,200	25,000
Computer Sciences	11,800	13,600	16,500	20,000	24,000
Agricultural Sciences	8,800	10,300	12,800	15,800	19,500
Biological Sciences	8,700	11,300	15,000	20,000	26,100
Psychology	10,500	12,300	15,000	18,500	23,700
Statistics	11,500	13,600	16,900	20,700	25,000
Economics	11,000	13,000	16,300	21,000	27,000
Sociology	8,500	10,400	13,000	16,700	21,000
Political Science	9,300	10,700	13,100	18,000	23,500
Anthropology	10,700	12,000	14,700	18,900	23,000
Linguistics	9,000	10,500	12,500	16,400	20,700

Source—National Register of Scientific and Technical Personnel, 1970.

COMPUTERS

Honeywell's New Range

THE recent announcement by Honeywell of a new range of computers implies that the company's acquisition of the business computer interests of General Electric (US) has already paid dividends. Honeywell claims that its new '6000' computers, which are closely related to a series which was nearing production at General Electric before the merger, will give at least 15 per cent more computing power than the IBM machines. And if the IBM policy of "unbundling" (that is, charging separately for software, maintenance and so on) is fully taken into account, the advantages of the Honeywell range could turn out to be much greater. The larger members of the new series also seem to have considerable advantages in computing power over the largest of the ICL '1900' series; the most powerful of the System 4 series made by ICL (the '4/72') is equivalent to the middle members of the '6000' family (the '6030' and '6040'). Honeywell obviously hopes to increase significantly its share of the British market but the company would be the first to admit that, in the public sector at least, it will have difficulty unseating ICL from its entrenched position.

Three members of the '6000' series have been specially designed for a mixed scientific and business workload but the other three can offer useful increases in computing capability for customers who will principally be using COBOL, the business language. Honeywell claims that the new series is the first to operate in all the four computing "dimensions", remote and local batch processing, time sharing and transaction processing (of which a good example is the storage of medical records). The four largest systems will also be available with as many as four central processors linked together in such a way that a fail-safe situation is achieved as well as increased throughput; the failure of one processor will no longer have a catastrophic effect.

Programs written for the 6000 series will be compatible with the smaller Honeywell 600 series, but compatibility of peripheral equipment with models made by other companies remains something of a thorny problem. At least one step in the right direction is the adoption of the COBOL programming language by the American Standards Institute as the recommended language for business machines.

Forecasts of the burgeoning state of the computer industry suggest that the value of computers installed throughout the world will double in the next five years to a staggering £31,000 million. With a ten per cent share of this market, Honeywell is well placed to take advantage of the boom, but the company will have to go a long way to make much impression on the dominance of IBM.

NEWS AND VIEWS

Human Breast Cancer Virus?

In mice, breast cancer (mammary adenocarcinoma) can be caused by a virus, the Bittner virus, which has an entirely characteristic and until now unique morphology. But on page 611 of this issue of *Nature*, Moore and his co-workers in Camden, New Jersey, Detroit and Bombay report the detection of particles, the morphology of which is identical to that of the Bittner virus, in many samples of human milk. The implications of this enthralling observation must be obvious to everybody—these particles in human milks may well prove to be the causative agents of human breast cancer, human breast cancer viruses, which can transform target cells in breast tissue when those cells occur in particular hormonal environments. In other words human breast cancer, like the murine disease, may well be initiated by a virus but promoted by humoral factors, in particular sex hormones.

Moore and his colleagues have detected this particle in seven out of one hundred and fifty-six samples of milk from Philadelphia women with no history of breast cancer in their families, in six out of ten milks from American women whose near female relatives had the disease and in eighteen out of forty-six milks from Parsi mothers living in Bombay. Although the size of the sample of milks from American women belonging to families with a history of the disease is small—no doubt because of the logistical problems of locating such women in lactation—the 60 per cent incidence of virus can hardly on that account be dismissed as insignificant. Similarly among Parsi women in Bombay, members of an inbred community of about 80,000 descended from Persian Zoroastrians who fled from Persia to escape religious persecution in the mid seventh century AD, the age adjusted incidence of breast cancer is at least 1.7 times that of the entire female population of Greater Bombay. And 39 per cent of the samples of Parsi milks contained detectable amounts of virus.

It seems likely therefore from these first data that more extensive samplings of milks from women of various categories and communities will reveal a correlation between high incidences of this virus-like particle in milks and individual risk of breast cancer. The correlation is unlikely to prove simple, however, for although breast cancer is more common among Parsis than other Bombay women, the age adjusted incidence of the disease is greater among English and Norwegian women, for example, than among Parsis. As with its murine counterpart the human milk virus may prove to be necessary for breast cancer to develop but not a sufficient factor to cause the disease.

Proof that murine breast cancer can be caused by the Bittner virus involved a fascinating but protracted series of inbreeding and cross breeding experiments; these established that some factor in milk transmits the cancer. Subsequent extensive investigations of mouse milks were made in an attempt to determine the identity of the agent and only recently have these culminated in the proof that one specific particle—the Bittner or mouse mammary tumour virus—is the aetiological factor. Although this virus is usually transmitted from mother to offspring in the milk rather than through the placenta or through the egg and sperm, it is significant that at least in some strains of mice the viral genome can apparently be transmitted in the sex cells.

Comparable breeding experiments with human populations are obviously out of the question and epidemiological statistics correlated with the results of screening tests for the human milk particle will no doubt prove, as usual, to be only a contentious and inadequate substitute. Marshalling a body of experimental and therefore circumstantial evidence sufficient to convince the sceptically inclined that this human milk particle is indeed a breast cancer virus is likely to prove equally problematical. The sort of evidence that is needed will include proof that human breast cancer cells contain virus-specific antigens or viral nucleic acids, that the cancer cells produce the virus, that the virus can transform cells in culture or induce breast tumours in animals and, most convincing of all, evidence that it is possible to vaccinate against the virus and lower the incidence of the cancer as a result, always assuming the human virus is not transmitted until after birth. Each of these criteria is bound to be extremely difficult to establish, not least because it has so far proved impossible to find a cell which can be transformed by or supports the replication of Bittner virus and the human virus will probably prove to be equally fastidious. Bittner virus has to be assayed in mice; quantitative investigations of the human virus will depend on finding some susceptible animal or cultivated cell.

Apart from further investigations of samples of milk there are, however, several obvious experiments that might be done as soon as enough of the human virus has been collected. Tests can be made to see if the particles contain reverse transcriptases and attempts should be made to establish whether or not the human virus and the Bittner virus share a common intergroup specific antigen, for such a common antigen has been found among the various mammalian sarcoma and leukaemia viruses. It would also be worthwhile testing to see if antisera against the Bittner virus antigens inhibit the reverse transcriptase activity, if one is detectable, in the human virus; such an experiment involving sarcoma and leukaemia viruses of different species is already afoot. Further experiments along the lines of those reported by Charney and Moore on page 627 of this issue of *Nature* are also called for. They have incubated Bittner virus with sera taken from women who have had breast cancer or, as a control, normal women, and then assayed the tumorigenicity of the treated virus. They claim to detect a statistically significant neutralization of the murine virus by the sera of the cancer patients, although it is debatable whether or not great reliance should be attached to the differences between averages of such a limited set of data. Notwithstanding their limitations, however, these experiments indicate one approach to establishing the serological relationships, if any, between the human virus and the Bittner virus.

There remains, of course, perhaps the most important but thorniest job of all. We shall not be able to get to grips at the molecular level with the biology of the mammary tumour viruses unless a susceptible cell which can be grown in culture is identified. There is no short cut. All the available cell lines will have to be tested.

But does the discovery of this virus particle in human milks have any implications for the treatment of what is after all the most prevalent cancer of adult females in many populations? It has to be admitted that in the short term there are precious few. Charney and Moore's suggestion that it might be possible to immunize against human breast cancer using the mouse virus as immunogen will cause more than eyebrow raising in many a tumour immunology laboratory. If the chief route of transmission of the human virus is through milk it might conceivably be possible to mount screening programmes for the virus in milks, the results of which might indicate cases in which breast feeding should be discouraged. And if the baby's first contact with the virus is in its mother's milk it might just be possible to devise some immunotherapy. On the other hand, should the virus be vertically transmitted in the sex cells, as in some strains of mice, or by passage across the placenta, immunotherapy would almost certainly prove useless in the face of immunological tolerance. Indeed, the problems of dealing with any vertically transmitted virus disease are at present intractable. It remains, however, an article of faith among tumour virologists that an understanding of the cause of cancer should at least facilitate the design of tailor-made chemotherapeutic agents. That, and the possibility that a screening procedure for this human virus in milk might provide another parameter for the early diagnosis of breast cancer, provides a realistic perspective to these most exciting discoveries.

Bright Future for European Particle Physics

Now that the final decision to build a large proton accelerator in Europe has been taken, it is only natural to speculate about the steps forward which may be achieved in elementary particle physics during the next decade or so. Many physicists, however, will point scathingly at the apparent plethora of expensive high energy devices now working or planned throughout the world. How is it possible to justify on scientific grounds the construction of the intersecting storage rings at Geneva, the 200 GeV synchrotron at Batavia and now the accelerator at Geneva ?

There is no one word answer to this, of course, but a number of justifications can be put forward. Both the existing CERN and Brookhaven machines have been producing protons of comparable energy (about 30 GeV) for more than ten years and one would have been forgiven for suggesting at their inception that there would be wastage of money and resources. As it turned out, nothing has been further from the truth and both laboratories are continuing to make maximum use of their available potential with few signs of repetition.

Experience with the CERN machine in particular should convince those persons who require a definite statement of scientific intent that not only is such a statement difficult to formulate but also it will almost certainly be changed out of all recognition as time passes. The CERN machine was conceived originally as a means of searching for the antiproton but the antiproton was discovered before it was even commissioned.

The intersecting storage rings at CERN must now be regarded very much as a window on the future; to a great extent the programme of research at the new accelerator will be determined by what is discovered with them. In fact, the decisions whether or not to increase the 300 GeV to 400 GeV and eventually to 800 GeV by adding and changing magnets may of necessity depend on the experiments at the storage rings.

Having made the point that all the best laid plans are likely to be modified by future events, there can be little harm in indulging in some crystal gazing. One of the chief questions which particle physicists would like to answer is not how, but why, some particles can be so successfully classified by the SU(3) and SU(6) group theoretical approaches which have dominated high energy physics recently.

Some particles have been theoretically predicted—not always from SU(3) and SU(6)—but have not so far been detected experimentally. The discovery of these could well be an important contribution from the new accelerator. The controversial quark, in which most physicists find it hard to believe because of its non-integral electronic charge, is an obvious candidate for an intensive search; it may be, however, that the quark is discovered before the European accelerator comes into operation and, in that case, quark physics will become one of the important fields of experimental study at the accelerator from the beginning.

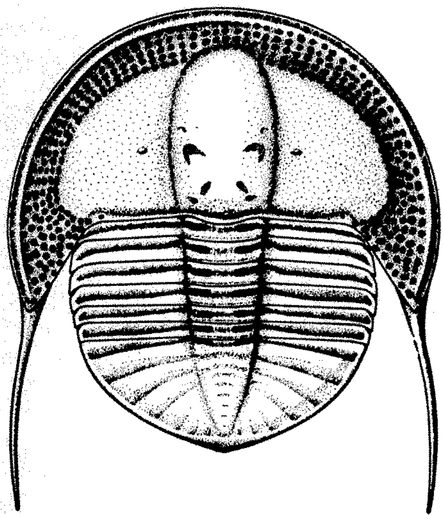
Many physicists have a much deeper and more intuitive belief in the intermediate boson which is thought to mediate the weak interaction (responsible for the decay of many semi-stable particles) in much the same way as the photon mediates the electromagnetic interaction. If it exists, this boson can almost certainly be produced in neutrino interactions and is being actively searched for in neutrino beams at accelerators throughout the world. Pairs of intermediate bosons can also theoretically be produced in proton–proton interactions and there is the distinct possibility that they may first be seen at the Geneva storage rings.

The Dirac magnetic monopole is yet another candidate for revelation by either the storage rings or the 300 GeV accelerator, but it has not excited sustained interest over the years and the interactions which might produce it are not really known. Its signature would be very characteristic, however, because its ionizing power at relativistic speeds is thought to be about 10^8 greater than any other charged particle.

Perhaps the most exciting advance will be a revelation of the structure of the nucleon. It is already clear from electron and neutrino scattering that the nucleon structure is granular and that the grains have a distribution of masses. Some theoreticians have explained this "granularity" in terms of the quark, and yet others have suggested that they are manifestations of new particles called partons. The situation is curiously similar to that in which Rutherford found himself earlier in this century.

TRILOBITES

An Australian Trinucleid



A new genus and species of trilobite—an extinct marine arthropod which flourished in the early Palaeozoic—has been recovered from Upper Ordovician siltstones near Parkes in New South Wales. According to K. S. W. Campbell and G. J. Durham of the Australian National University (*Palaeontology*, **13**, 572; 1970), it is the first member of the family Trinucleidae to be described from Australia. They have given it the name of *Parkesolithus gradyi* and this figure shows their reconstruction which illustrates the trilobite's semicircular cephalon with its unornamented spines and the six-segmented thorax.

RODENTICIDES

The Search Continues

from a Correspondent

In Britain, at least, some far reaching changes in the control of rodent pests are on the way, as a result of the development of resistance to anticoagulant rodenticides. Some of these changes were discussed at a symposium on rodenticides held by the Pesticides Group of the Society of Chemical Industry in London on February 15.

In the first contribution, Mr R. Scott (Royal Borough of Kensington and Chelsea) suggested that, besides resistance, the casual manner in which anticoagulant rodenticides were used was an important element in the complex of factors contributing to current increases in infestation by the urban house mouse. This theme was continued by Mr J. H. Greaves (MAFF, Pest Infestation Control Laboratory) (PICL), who pointed out that the apparently inexorable spread of populations of resistant rats which now occupy some thousands of square miles of agricultural land in Britain has arisen largely from the continued use of anticoagulants in the affected areas, a practice which has been unavoidable in the absence of alternative rodenticides that are equally safe and convenient to use.

Dr A. D. Martin (PICL) suggested several physiological mechanisms in rodents which may be open to attack by particular classes of compounds. Among his favourites were new types of anticoagulants and antimetabolites of nicotinamide, but the list included drugs with immunosuppressive, hypoglycaemic and anticorticosteroid activities and many others. Two intriguing suggestions were that the target species might be presensitized or that rodenticides could be potentiated by the respective use of inducers or inhibitors of metabolizing enzymes. The problems, however, of developing basic ideas of this sort were vividly illustrated by further contributions which showed that relatively little progress in specific lines of research had so far been made. This research has included attempts to upset thermoregulation in the mouse (Mr R. A. Davis, PICL) and to remove the limitations of alphachloralose as a rodenticide (Mr J. O. Bull, Rentokil Laboratories) through the use of a combination of compounds.

Dr P. B. Cornwell (Rentokil Laboratories) went on to describe an extensive series of experiments aimed directly at securing improvements in existing rodenticides through the application of microencapsulation techniques. He concluded, however, that though the principle might be valid, basic improvements in the characteristics of release of the microcapsules were needed to yield results of practical value.

The door was held open to a possible, if unpredictable, quick success by Mr F. P. Rowe (PICL), who described a screening project in which compounds submitted by industry are tested for rodenticidal activity on a confidential basis. Doubts were expressed about the immediate commercial prospects for new rodenticides, for resistance is not yet sufficiently widespread to create a major

Picking Up Chick Genes

When an inert nucleus from a chicken erythrocyte is introduced by cell fusion into the cytoplasm of a different cell type derived from another species, it resumes synthesis of nucleic acid and chick specific proteins. Finding out how the chick genes are reactivated is, in itself, an exciting enough prospect, but in next Wednesday's *Nature New Biology*, Harris and his colleagues at Oxford take the technique a stage further by introducing genetic material from chick erythrocytes into nuclei of mouse cells.

The chick nuclei were introduced into the cytoplasm of mouse A9 cells by the now conventional means of inducing cell fusion with ultraviolet inactivated Sendai virus. The mouse cell strain lacked the enzyme inosinic acid pyrophosphorylase, but the chick cells were derived from birds which did not have this disadvantage. The hybrid cells were then grown up in a medium in which cells lacking this enzyme activity die.

Only cells in which the chick erythrocyte nucleus has been reactivated can therefore survive in this medium. But within three or four days of the cell fusion, the heterokaryons enter a mitosis during which the erythrocyte nuclei disintegrate. Any cells which survive after this time must therefore have a functioning chick gene for inosinic acid pyrophosphorylase, presumably located on a chromosome inside the mouse nucleus. The corresponding enzymes synthesized by mouse and by chick can be distinguished by their electrophoretic properties, so Harris and his colleagues were able to show that the survival of cells in the selective medium did indeed result from the synthesis of the chick-coded enzyme.

But looking at the chromosome constitution of the surviving cells showed that no chick chromosomes were present. This implies that during the disintegration of the chick erythrocyte nucleus, some of its genetic material has been incorporated into the mouse chromosomes. That there must be very little such chick material was shown by testing the cells for chick specific antigens on their surface; this is a very sensitive test indeed, and the genes which determine these antigens are widely dispersed on the chromosomes of the chick cell. No such antigens could be found on the surface of these cells, which implies that the extent of chick material picked up by the mouse nucleus must be very small indeed.

What is the state of the chick genetic material in the mouse nucleus? Is it integrated into the mouse chromosome or is there some other form of attachment? The rate at which the gene coding for inosinic acid pyrophosphorylase is lost from cells can be estimated by transferring cells into a normal medium in which the enzyme is no longer needed for survival, and then transferring to a medium which selects against cells which produce the enzyme. This gives an estimate of the number of cells that have lost the enzyme activity during growth in the normal medium. Normal mouse cells lose the enzyme at a frequency of less than 1 in 10^6, but in the hybrid cells the frequency was 20 per cent.

This means that the chick genetic material has been only loosely integrated into the mouse cells. Harris and his colleagues have not yet shown conclusively that the chick genetic material is in the nucleus of the mouse cell, but it seems unlikely that it has remained in the cytoplasm.

new market. These doubts were reflected in the news that the World Health Organization is also sponsoring research on new rodenticides and they gave added force to the view that continuing support in the public sector is necessary for progress in this small but active and disproportionately important field of research.

RESERVOIRS

More Midges, More Fish?

INCREASING by artificial means the number of midge larvae in a reservoir seems a topsy turvy way of providing drinking water free of foreign bodies. Investigations by the Inland Fisheries Branch of the State of California Department of Fish and Game suggest, however, that midges and drinking water are not so incompatible as they might seem (*Fish Bull. Calif.*, No. 148; 1970). Midge larvae are important in the food chains of certain fish. Increasing the numbers of these larvae should therefore, in theory, provide more food for fish, and ultimately better fishing. If this can be done by a method of artificial destratification of the water, a practice incidentally which also improves the quality of water, the water authorities should be in business. It was an experiment which the California Department of Fish and Game thought worthwhile.

Midge larvae, together with tubificid worms, nematode worms and certain species of mollusc, are typical bottom dwelling animals of all freshwater lakes and reservoirs. But in summer months their distribution is limited and they may be absent from the deeper parts because the water there can become deoxygenated and the bottom muds are often toxic. This state of affairs is found particularly in lakes and reservoirs which are rich in nutrients (what limnologists call productive or eutrophic bodies of freshwater) and arises from a combination of physical factors.

In summer months when there is comparatively little wind to stir up the water, the upper layers warm up more quickly than the lower regions and a sharp division in temperature—a thermocline—is formed. Decomposition of organic matter in the deepest parts uses up the oxygen, and toxic materials accumulate in the mud at the bottom. At certain depths therefore the reservoir or lake becomes divided into a lower, anaerobic cool layer or hypolimnion and an upper, warm aerobic epilimnion. In a particularly productive reservoir in which a large part of the water is deoxygenated, the water is obviously not very suitable for drinking and abstractions can then be made only from the epilimnion. One solution is to destratify such reservoirs artificially by injecting compressed air and the California Department of Fish and Game has already shown this to be feasible; it improves the quality of water by making the temperature and oxygen concentrations relatively uniform throughout the year. But how does destratification affect the bottom organisms such as midge larvae, which in a sharply stratified reservoir are presumably excluded from the toxic deep parts and therefore less available as food for fish? The department decided to investigate this problem in El Capitan Reservoir in San Diego County. The reservoir was destratified in 1965 and was not allowed to stratify again until 1967. The bottom organisms were sampled by dredging in 1964 before destratification and in 1965, 1966 and 1967.

During destratification midge larvae, oligochaete worms, nematode worms and clams rapidly invaded the deepest regions in summer and their total numbers increased dramatically. In stratified conditions in 1964, for example, midge larvae were practically absent below a depth of 10 m by July; in 1966 there were substantial numbers at 25 m or more. The oligochaetes and the nematode worms fluctuated in a similar manner.

It seems likely that a combination of factors—ample oxygen and food and warmer temperatures—led to the changes in the populations of bottom organisms, rather than oxygen alone. The El Capitan results certainly indicate that artificial destratification might retard or reverse natural eutrophication in such waters and make them less productive. This could, in theory, have a limiting effect on fish populations. On the other hand, changes in the distribution of food, such as midge larvae, and the better environmental conditions for fish in the hypolimnion in summer might more than counterbalance a minor decrease in productivity. This is a long term implication. Meanwhile, the California Department of Fish and Game is considering using artificial destratification in reservoirs like El Capitan as an alternative to heavy treatment with copper sulphate which is often used to remove algae and to make the water drinkable. This substance, it says, can have much more immediate effects on fish populations far worse than anything to be expected from destratification.

Another Biological Control Mechanism

MOST molecular biologists would agree that a given structural gene dictates the amino-acid sequence of a protein and that, given this sequence, the polypeptide chain will fold itself into the "native" structure. In the case of proteins comprising more than one polypeptide chain there is, of course, the extra stage of subunit assembly. In next Wednesday's *Nature New Biology*, M. Rosenberg presents some findings which indicate that subunit assembly can be tissue specific inasmuch that different distributions of lactate dehydrogenase (LDH) isoenzymes are observed in different tissues although the component subunits are the same. The LDH molecule is known to be tetrameric and isoenzymes arise from the fact that different subunits, A and B, assemble to give molecules of the structure A_4, A_3B, A_2B_2, AB_3 and B_4. If the assembly of equal numbers of A and B chains is random, then these forms will occur in the binomial proportions of 1 : 4 : 6 : 4 : 1.

In mammalian tissues there are usually five distinct isoenzymes although the distribution varies from tissue to tissue for a given animal. Rosenberg claims that this differential tissue distribution in mammals is explained simply by there being excess of one subunit over the other as a result of differential rates of synthesis of the two types of chain. In a number of fish, however, Rosenberg has found that there are only one, two or three isoenzymes and in fish with five isoenzymes the distribution is non-random. She was able to take a three isoenzyme mixture from the common mackerel (*Scomber scombrus*) and dissociate and reassociate it *in vitro* to give all five isoenzymes. Their relative migrations in an electric field indicated that the three isoenzymes in the original mixture were A_4, A_2B_2 and B_4 and this was confirmed by immunochemistry. Rosenberg showed in similar fashion that two isoenzyme fish LDH was A_4 and B_4 and one isoenzyme LDH was A_2B_2.

The differential distribution of isoenzymes in different tissues of the same organism was well illustrated by the alewife (*Alosa pseudoharengus*) which had two, three and five isoenzymes in different tissues. Controls indicated that failure to observe the missing structures was not related to the fact that they were preferentially degraded in the extraction procedures.

Rosenberg concludes that the missing isoenzymes are absent because their dissociation rates are disproportionately high and that this could be a function of the different concentrations of ions, proteins and coenzymes in different tissues. Rosenberg's findings complement the statement by Jaenicke (in *Pyridine Nucleotide Dependent Dehydrogenases*, edit. by H. Sund, p. 70; Springer-Verlag, Berlin and New York; 1970) that the primary structure in conjunction with the specific solvent conditions is the major determinant of the three-dimensional structure up to the level of quaternary structure. The mode of subunit assembly is thus potentially a further source of control in biological systems.

PROTEIN SYNTHESIS

The Captive Messenger

from our Molecular Biology Correspondent

WHETHER the particles of rapidly labelling RNA and protein that have been seen in the cytoplasm of mammalian cells are fact or artefact is still regarded in the more sober quarters as an open question, and so indeed is their relation to the complexes containing messenger RNA that are released when polysomes are dissociated. That labelled RNA comes away in sizable particles of high buoyant density has been known for some time, but the possibility that the RNA picks up basic proteins when dunked in the cytoplasm cannot be disregarded. Such random association was indeed shown to occur last year by Baltimore and Huang.

The nature of the complexes present in rat liver polysomes has now been re-examined by Lee and Brawerman (*Biochemistry*, **10**, 510; 1971), who report as follows: Treatment with EDTA releases pulse labelled RNA in the form of a highly polydisperse population of particles. The same effect could be produced in other ways—by raising the *p*H at defined potassium and magnesium concentrations and by treatment with urea. Free messenger cannot be liberated by urea or by high ionic strength, and the particles differ in this respect from the non-specific, and presumably adventitious, complexes described by Baltimore and Huang. Treatment with sodium dodecyl sulphate, which is one of the most efficient reagents for breaking up complexes between proteins, is the only satisfactory method so far known for extracting the free messenger. The latter has a much smaller sedimentation coefficient than the complex, which moreover is the same no matter from which fraction of the broad sedimentation profile of the complex it has been extracted.

The question remains whether the associated material consists of proteins torn out of the ribosomes on dissociation, or of components that the messenger carries into the cytoplasm. The first and more obvious explanation is supported by an observation of Nolan and Arnstein, who found that a poly U messenger carries ribosomal protein away with it on dissociation of the ribosomes. On the other hand, Lee and Brawerman refer to work of their own, as yet unpublished, according to which ribonuclease-treated ribosomes, when exposed to EDTA, release that part of the messenger which is shielded against the nuclease, in uncomplexed form. They also report that in a similar mammalian system, the complexes are found after the ribosomes are allowed to run off the messenger.

It may be remarked that it has not even been properly demonstrated that the associated material is protein, and there is at this stage little that one can say about the possible purpose of this luggage that the messenger seems to carry around the cell. Lee and Brawerman suggest that it is unlikely to be anywhere but at the end of the molecule if it is not to impede the translation process, and that it may be nothing more than a part of the cell membrane to which the polysomes are normally tethered. It will be recalled, however, that descriptions have been published of ribosomal proteins that attach the ribosome to the membrane.

Another unexpected feature of a eukaryotic messenger is reported by Gaskill and Kabat (*Proc. US Nat. Acad. Sci.*, **68**, 72; 1971). They have prepared rabbit haemoglobin messenger from polysomes, and examined it electrophoretically in polyacrylamide gels. In this medium it separates from various contaminants and degradation products and can be unequivocally identified by its labelling properties. There follows something of a leap of faith in that the authors determine the molecular weight from the electrophoretic mobility in the gel. This method in general seems to give reliable results, but would be expected to fail for species with very different degrees of base-pairing from those of the standards in terms of which the calibration is set up. A graphic example of such an effect is to be found in a recent article by Groot, Aaij and Borst (*Biochem. Biophys. Res. Commun.*, **41**, 1321; 1970), who find that with mitochondrial RNA the measured molecular weight changes by 40 per cent relative to calibration standards, according as the measurements are made at 2 or 28° C. This reservation aside, however, Gaskill and Kabat's results at least suggest that the messenger is more than half as long again as it need be to code for the globin chains. This may relate to the battery of stop and start and perhaps other signals that Sanger and his colleagues found in the polycistronic R17 viral RNA.

Heterogeneity of Antigenicity in Malignant Cells

CANCER research wends a tortuous path reflecting the many basic uncertainties in our understanding of the genetic control of differentiation of metazoan cells. Relatively recently, studies in which malignant and normal cells were hybridized revealed that a malignant genotype could apparently be masked in the presence of a normal complement of genetic material (Harris *et al.*, *Nature*, **223**, 363; 1969). The same series of experiments suggested that certain malignant cells had the ability to hide the transplantation antigens of the normal cell constituent of hybrids. The inference from this second finding was that tumours which had been transplanted a long time could enhance their capacity to grow malignantly by effective reduction of antigenicity. Such a mechanism could be thought of as involving antigenic simplification by genetic deletion or, alternatively, a modification process could be implicated by which the activity of these genes, which determine the transplantation antigens, could be quantitatively reduced. Modifier genes are familiar to botanists as a common feature of the genetic changes involved in speciation.

A further set of experiments described in next Wednesday's *Nature New Biology* is relevant to this theme. Negroni and Hunter have amplified an earlier finding (E. J. Walls and G. Negroni, *Europ. J. Cancer*, **2**, 221; 1966) that a clone of cells, isolated from a polyoma induced fibrosarcoma, though itself non-malignant can effectively immunize against the growth of a similar but malignant cell population. The evidence is compatible with the notion that the non-malignant cell population is more antigenic than the malignant cell clone but has a qualitatively similar antigenicity. Negroni and Hunter go on to show that malignant cell clones can be derived from the "non-malignant" cell line by selection with an immune antiserum (produced in C3H mice by immunization with the non-malignant cell lines). The same antiserum applied to certain malignant cell populations effectively reduced immunosensitivity among the survivors.

The phenomenon of tumour progression, by which is implied a change in growth potential with time, has been recognized for many years and a summary of its ramifications has recently been published (L. Foulds, *Neoplastic Development*, **1**, Academic Press, London and New York, 1969). It seems possible that the heterogeneity of antigenicity among malignant cell populations such as that described by Negroni and Hunter is an aspect of tumour progression and a singularly interesting corollary is that, if non-malignant variants could be selected and grown from among a tumour cell population, it is possible that they could be used as a means of immunizing against the truly malignant cells. It is also tempting to wonder whether the "non-malignant" characteristic which, according to the earlier information, involves a lack of the capacity to liberate virus in culture and normal contact inhibitory behaviour really is non-malignant. Would these cells which display such meek characteristics in normal adult mice betray a malignant nature in immunologically deprived recipients? If they did, it would be necessary to define malignancy as a state resulting from a particular tumour–host relationship; a long overdue alteration in immunologists' thinking.

STROMATEOID FISHES

Life with Jellyfishes

from our Marine Vertebrate Correspondent

THE stromateoid fishes are a widely distributed group of temperate and tropical marine fishes found in a range of depths in inshore and oceanic waters. Perhaps one of the best known, a member of the family Nomeidae, is the Portuguese man-of-war fish, *Nomeus gronovii*, which is found under the float of the siphonophore *Physalia* swimming actively among the toxin-laden tentacles. Their apparent immunity to the toxin produced by the stinging cells has aroused considerable interest, and one report suggests that they can survive as much as ten times the dose of *Physalia* toxin that would kill a fish of comparable size. In spite of this relative immunity *Nomeus* seems to avoid contact as much as possible with the tentacles. Many other stromateoids are known to similarly associate with jellyfishes and siphonophores.

Stromateoid fishes show marked changes during growth, and the body form of young fishes is often markedly dissimilar to that of the adults. The differences are not all external, however, for although most lack a swimbladder when adult, they possess a functional one as juveniles. Dr Michael H. Horn has discovered that in fourteen out of the fifteen recognized genera of stromateoid fishes the swimbladder regresses with age (*Breviora*, No. 359, 1; 1970). The exception is the largely coastal genus, *Pampus*, which seems to have no swimbladder at any age, and is believed not to associate with jellyfishes when young.

The swimbladder in these fishes is a hydrostatic organ and, even if small, provides a degree of buoyancy. During their young stages the skeleton is poorly ossified and the musculature may not be well developed, and thus the juveniles probably have a lower specific gravity than the adults, and even a small swimbladder will take them close to neutral buoyancy. The reduction of the swimbladder with growth is gradual, the sac diminishing slowly until it is completely resorbed.

The interest in these observations lies in their relation to the biology of these fish. In the American Atlantic coast butterfish, *Peprilus triacanthus*, the swimbladder has completely regressed by the time that the fish is 10 cm in body length, and it is at about this size that the young cease their association with jellyfish medusae. Butterfish smaller than this length swim by hovering close to the medusa, whereas larger specimens do not hover but swim continuously. The pectoral fins increase in size with age and are used extensively for propulsion by the larger fish. It seems that continuous swimming with some propulsion by the pectoral fins is the general way of life for adult stromateoids.

Nomeus, the stromateoid which associates with the siphonophore *Physalia* in a more intimate and enduring way than its other relatives, retains a functional swimbladder at a greater length than other stromateoids. It is not known whether *Nomeus* remains with *Physalia* throughout its life, but specimens as large as 143 mm body length have been captured at the surface with *Physalia* and possess a large swimbladder.

Horn's study shows that the possession of a swimbladder in the young stages could be a positive advantage to a fish which lives under jellyfish medusae, or among the toxin-laden tentacles of a siphonophore, floating at the surface. An ability to stay afloat efficiently and manoeuvre with nicety in such a microhabitat is as obvious an advantage to the small fish as the greater swimming capacity of adults living in deep water in the open ocean.

Carbohydrate or Protein in Transplantation ?

Sanderson, Cresswell and Welsh suggest in next Wednesday's *Nature New Biology* that the antigenic determinants responsible for exciting immunological responses to tissue and organ grafts are predominantly carbohydrate rather than protein. Using human spleen tissue from individuals known to possess three quite distinct transplantation (histocompatibility) antigens (Bt 4, Bt 5 and Bt Walde), Sanderson *et al.* prepared glycoprotein fractions by digestion of cell membranes with papain and purification with the aid of chromatography and disc gel electrophoresis. These soluble materials, each with a molecular weight of approximately 45,000, were further digested with insoluble pronase and the resulting glycopeptides were separated from the bulk of the amino-acids and peptides by chromatography on 'Sephadex G-50'. A low molecular weight (probably 8–10,000) fraction with a very high carbohydrate content was obtained for each specificity and was found to be serologically active in that it inhibited the lytic action of the specific antiserum. The glycopeptides of this fraction had a restricted range of amino-acids which always included aspartic acid, serine and threonine—all of which are especially concerned with linking sugar to protein.

At first sight these data seem to be irreconcilable with the now widely held view that the specificity of the "strong" histocompatibility antigens—the antigens controlled in man by the HL-A and in the mouse by the H-2 locus—depends on the amino-acid sequence of glycoproteins. This notion stems largely from the work of Shimada *et al.* (*Proc. US Nat. Acad. Sci.*, **65**, 691; 1970), who analysed and compared tryptic digests of glycoproteins obtained from mice carrying two distinct H-2 specificities. Although 90 per cent of the peptides were identical, each preparation had some that were unique, whereas no detectable differences were found in the composition of their carbohydrate moieties (Nathenson, *Ann. Rev. Genet.*, **4**, 69; 1970). The weakness of these experiments is that Shimada *et al.* did not subject their fractions to biological tests such as *in vitro* inhibition of antibody, and that the amino-acid differences found by them could be unrelated to the activity of immunodeterminants that may form only a very small portion of the glycopeptide molecules. Nevertheless their data, together with those from other laboratories, seem to implicate protein quite strongly. The carbohydrate hypothesis, on the other hand, derives support from the observation that mouse (Billingham *et al.*, *Transplant. Bull.*, **5**, 377; 1958) and human (Sanderson and Cresswell, in *Transplantation Antigens and Tissue Typing*, edited by Elves and Nisbett, p. 87; Oswestry Orthopaedic Hospital Management Committee, 1969) histocompatibility antigens can be largely inactivated by periodate treatment, and that there are serological cross-reactions between mouse H-2 antigens and pneumococcal polysaccharide type XIV as well as human blood group A substance (Brent *et al.*, *Brit. J. Exp. Pathol.*, **42**, 464; 1961).

In an attempt to reconcile their own data with those pointing to the role of protein, Sanderson *et al.* suggest that although the specific determinants may be composed of carbohydrate they are carried on a molecular peptide backbone that plays a crucial part in the spatial arrangement of the determinants and therefore, indirectly, in determining their specificity. This is an interesting idea which has already been considered in relation to the mouse H-2 antigens (Shreffler and Klein, *Transplant. Proc.*, **2**, 5; 1970), but further work is needed to test its validity. Will these low molecular weight glycopeptides prove to have biological activity other than the ability to inhibit antisera; for example, can they sensitize or induce tolerance? Whatever the answer, Sanderson *et al.* have made it clear that carbohydrate is not merely an accidental contaminant of histocompatibility antigens, and that it is likely to have a highly specific function.

NUCLEAR PHYSICS

Symmetric Fission

THE continuing competition to produce new nuclear species is providing more material for studies of the properties of fissioning nuclei, even though the pace in this branch of nuclear research is perceptibly slower than in the 1940s. Elements up to 104 or maybe 105 have been synthesized and there is talk that element 112 may have been produced (Marinov *et al.*, *Nature*, **229**, 464; 1971). In 1963 it was noted in studies of spontaneous fission of artificially synthesized elements that the average mass of the heaviest fragment remained constant at $A = 142 \pm 1$, while the mass of the light fragment increased when a range of nuclei from curium 248 ($_{96}\text{Cm}^{248}$) to fermium 254 ($_{100}\text{Fm}^{254}$) was considered (R. Brandt *et al.*, *Phys. Rev.*, **131**, 2617; 1963). If this trend were to continue a truly symmetric fission would not be obtained until the nuclear mass approached $A = 284$. There has been speculation, however, that symmetry would be obtained at some lower mass where the characteristic strong binding energy associated with the nuclear magic numbers 50 and 82 manifests itself. Briefly, this arises from the fact that some nuclei with certain numbers of neutrons and protons are particularly stable. These are found experimentally to be 2, 8, 20, 28, 50, 82, and 126. A nucleus which has a magic number of neutrons and of protons, but not necessarily the same number, is termed doubly magic and is an even more energetically bound species. The values of the magic numbers are understood theoretically in terms of a neutron or proton moving in an average potential well formed by the other particles in the nucleus with the inclusion of a strong spin-orbit interaction. The resulting solution which gives the quantum levels of the particle in the potential well has well defined energy gaps at the magic numbers.

The fission fragments should therefore show some trend towards symmetry as the fissioning nucleus approaches $_{100}\text{Fm}^{264}$, which is composed of exactly two tin 132 ($_{50}\text{Sn}^{132}$) nuclei, a particular isotope of tin that has a doubly magic structure. Such a trend has now been reported by a group from Los Alamos (J. P. Balagna *et al.*, *Phys. Rev. Lett.*, **26**, 145; 1971). They have studied the spontaneous fission of $_{100}\text{Fm}^{257}$ and observe a much greater degree of mass symmetry than for $_{98}\text{Cf}^{252}$ and $_{98}\text{Cf}^{254}$ which they also studied.

The results from Los Alamos constitute the first piece of evidence for symmetric fission in this mass region. There is one fact, however, that makes the generalization of this result a dubious matter. The isotope $_{100}\text{Fm}^{257}$ has an odd number of neutrons, so the properties of the fission are affected by the angular momentum and parity of the nucleus which is different from nuclei which have an even number of neutrons and protons.

The fission of one other nucleus with an odd number of particles has been studied in this mass region, einsteinium 253 ($_{99}\text{Es}^{253}$), and the results obtained for this nucleus are consistent with those of its neighbours which have an even number of neutrons and protons. This, of course, does not imply that the fission of $_{100}\text{Fm}^{257}$ is characteristic of its neighbours. A much better test, as suggested by the Los Alamos group, would be to study the spontaneous fission of some other heavy nucleus such as $_{100}\text{Fm}^{256}$ or mendelevium 258 ($_{101}\text{Md}^{258}$), or any heavier nucleus that may be available.

OCEAN FLOORS

More Nodules

from our Geomagnetism Correspondent

MANGANESE is not a particularly abundant element in the Earth, either within the crust or, if chondritic meteorites are any guide, within the deep interior. On average it forms only about 0.1 per cent of igneous rocks, compared with several per cent of iron; and because the manganese in oceanic sediments is ultimately derived from continental igneous rocks, concentrations there are not much different. All of which accounts for the great interest aroused by the discovery of manganese-rich nodules and slabs on the ocean floor. A typical nodule contains between 6 and 24 per cent manganese, about the same concentration as iron. Clearly, such nodules cannot be derived from continents unless some remarkable concentration process has occurred. Their origin is not actually known, though because of a close association with volcanic rocks it is likely that the manganese-rich material was derived from lava as it extruded into the seawater.

Not surprisingly, manganese nodules and slabs have often been viewed in economic terms. But there is one snag. Most deposits lie at depths of 18,000–20,000 feet or more and far from land—a situation guaranteed to turn businessmen, economists and mineral prospectors off. But deposits newly discovered in the Kauai Channel, Hawaii, by Maury Morgenstein of the University of Hawaii are likely to make an altogether different economic story. For manganese nodules and crusts have been found at depths of only 5,000–8,000 feet and lying only 5–8 miles offshore. Moreover, they cover at least an area of 150 square miles to a thickness of over 10 inches in places. In short, Morgenstein has discovered an economically important reserve which is relatively easy to get at and which is likely to have a profound effect on Hawaii's economy in the longer term.

In fact, the story may not end there. It is possible, of course, that Morgenstein has by accident hit on the only manganese deposits in the area. On the other hand, in the vicinity of Hawaii there is a total of 3,750 square miles of shallow seafloor with the same geological conditions as the Kauai Channel, all within ten miles of land.

London Ash Revealed in Harwich

NATURE is full of mysteries; but few are so mysterious as those which science could in principle have solved at any time during the past hundred years or so but did not. Nobody would pretend that the minor mystery unearthed and solved by G. F. Elliott, of the British Museum (Natural History), and reported in next Monday's *Nature Physical Science*, is likely to change the face of geology. But all the same Elliott must have obtained a peculiar satisfaction from it; and for that he can be envied.

The problem which Elliott has solved is the relationship between the so-called London Clay of southern England and the similar deposits in continental Europe. The continental clay is marked by a thin ash layer near the base; but, in spite of the many petrological studies, no comparable layer has ever been discovered in England. As a result some geologists have suggested that the ash fall never in fact reached England and others have taken the view that the two clay deposits were not at the same period of time.

It turns out that neither of these two assumptions are necessary. The London Clay which is exposed on the foreshore at Harwich contains a conspicuous stone band near its base. Indeed, this band has been known for more than two centuries, for in 1730 one Dale described it and noted that Harwich was paved with it. Elliott's studies now reveal that the missing ash is contained in this very stone band. Preliminary petrological examination of the ash suggests that it is very similar to that reported from the so-called London Clay in Denmark. It seems therefore that the English and continental ash layers are, after all, contemporaneous. The mystery is laid to rest. The English ash contains angular brown glass shards, some of which are streaky and resemble pumice, crystal fragments (often plagioclase) and lithic fragments full of opaque granules and containing minute, elongate feldspar crystals.

SELENOLOGY

Collapse Craters?

from our Geomagnetism Correspondent

LUNAR craters are, as every schoolboy knows, the result of meteoritic impact. But are all craters on the Moon impact craters? After all, the nature of the Apollo samples has been taken as evidence for the existence of lava flows on the Moon; and certain terrestrial lava flows contain craters of a different sort—volcanic collapse craters. Is it possible then that some lunar craters are caused by collapse rather than impact?

Terrestrial collapse craters are usually caused by deformation of partly cooled surfaces following withdrawal of fluid lava from beneath the crust during extrusion, or to drainage of surface material into subsurface cavities. If longitudinal structures such as fractures or lava tubes are present, the collapse craters produced are elongated and tend to form chains. If, on the other hand, there are no distorting structures the craters are circular and apparently distributed randomly. In other words, viewed from a distance they would probably be indistinguishable from impact craters. And so if there really are lava flows on the Moon it is reasonable to suppose that they, too, are liable to undergo collapse.

But short of close examination of the craters, how could such a hypothesis be tested? Greeley and Gault (*Science*, **171**, 477; 1971) have done it simply by comparing size-frequency distributions of lunar craters with those of known terrestrial collapse craters obtained under similar conditions. Thus, because the lunar counts were made from photographs of areas in and near Copernicus taken during Lunar Orbiter missions, terrestrial collapse craters in basalt at Modoc (California), Wapi Field (Idaho) and Laguna (New Mexico) were photographed at similar scales and under similar light conditions. The three terrestrial size-frequency distributions which resulted were similar and possessed two obvious characteristics—the maximum crater density is caused by craters in the range 8–12 m in diameter, and the slope of the cumulative crater density curve for craters of diameter greater than 10 m is about -3.

The first thing to be said about the lunar size-frequency distributions is that most of them are quite different from those on Earth. Distributions from the continuous ejecta blanket, the flat dark fissured portion of the floor, the smooth inner wall and the smooth terraces on the rim flanks of Copernicus are similar to each other, but the cumulative crater density curve for each has a slope of about -2. Distributions from the interior terraces ("flat, dark, smooth often fissured terraces which appear to fill low regions between slump blocks of the inner crater wall") and a floor fissure flow ("a small, smooth, relatively uncratered unit associated with fissures on the floor") are quite different, however. They are, in fact, very similar to the terrestrial collapse crater distributions; and have, in particular, cumulative curve slopes of about -3 and a maximum number of craters in the range 11–16 m diameter.

The conclusion to be drawn from all this, according to Greeley and Gault, is that many of the craters on the interior terraces and the floor fissure flow are collapse craters—a hypothesis put forward by Kuiper *et al.* some five years ago (*Calif. Inst. Tech. Jet Propul. Lab. Tech. Rep.*, 32–800; 1966). This could, of course, affect some indirect determinations of the age of the lunar surface. If lunar craters are caused by meteoritic impact, older surfaces will presumably have more craters than younger ones—a fact which can be used to assign relative ages to different parts of the lunar surface. But if a surface contains collapse craters in addition to impact craters, it will seem to be relatively too old.

Piecing Together the Life Stories of Meteorites

Two articles in Monday's *Nature Physical Science* may be signposts to the way in which a few of the holes in what is known about the immediate past history of meteorites will be filled in. The article by J. F. Lovering and his colleagues describes one of the few meteorites which has come near to doing anybody an injury—on the face of it meteorites have a surprisingly unimpeachable record considering that they are lobbed into the atmosphere at speeds of tens of kilometres per second. But on September 28, 1969, a meteorite fragment tore through the corrugated roof of a hay shed near Murchison, in Victoria, Australia, fortunately without striking anybody. The weight of meteorite fragments collected from the vicinity of Murchison after September 28, 1969, that have found their way into museums or the University of Melbourne adds up to 82.7 kg, but "a considerable quantity" is thought to have found its way into private hands, underlining the necessity for measures like that which has been laid before the British House of Lords to make all meteorites which fall in Great Britain crown property (see *Nature*, **229**, 446; 1971).

As well as giving a preliminary account of the Murchison meteorite, which seems to be a type II carbonaceous chondrite, the article by Lovering *et al.* raises the hope that an examination of the fragments will give details of how the parent body was shattered by the pulse of frictional heat as it struck the atmosphere. Apart from the intrinsic interest, the problem is significant because for determinations of meteorite age it is important to use fragments that have not been too much affected by heat. Most of the Murchison fragments have complete fusion crusts indicating that break-up took place while the meteorite was still moving fast enough to cause ablation. Some fragments have crusts of two thicknesses, the thicker presumably formed at an earlier stage in the fragmentation process.

In the second article knowledge of the effect of the heat pulse is carried a stage further by an examination of the Ucera chondrite which fell in Venezuela on January 16, 1970. The intensity of the thermoluminescence from samples of meteorite depends on the heating that the samples received in the atmosphere, samples taken from near the fusion crust showing weaker thermoluminescence than deeper material. J. E. Vaz reports a systematic examination of the thermoluminescence along two axes through the Ucera meteorite, from which it is inferred that the temperature at 4 mm inside the final surface exceeded 120° C but did not reach 240° C, and that deeper than 1.5 cm the temperature cannot have been more than 120° C. This seems to confirm laboratory studies of the transformation in the metals and silicates of meteorites which also indicate a depth of penetration of the heat pulse a centimetre or so.

As well as showing that the thermoluminescence output has not been affected by the heat pulse other than in the outer 1.5 cm of the Ucera meteorite, the thermoluminescence measurements along one axis show a slight asymmetry about the centre. For parent bodies that were originally less than 2 m across, which would include the Ucera meteoroid, thermoluminescence is induced chiefly by cosmic radiation. Thus it rather looks as if the asymmetry in the thermoluminescence distribution means that the meteorite was shielded non-uniformly while it was exposed to cosmic rays in space. Non-uniformity of the heating in the atmosphere cannot be the answer because the meteorite is well rounded, and because of the similarity of the thermoluminescence output from samples adjacent to the fusion crust on different sides. A shielding effect is also indicated by the comparatively low ^{14}C activity measured for the Ucera meteorite.

Oddly enough, for an old science that was under way in the last century, the study of meteorites is having a revival just now. Part of the story is a renewed interest in the determination of meteorite ages, but meteorites should also provide some kind of record of the past history of the cosmic ray flux.

Problems facing University Science

F. R. JEVONS

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Professor Jevons gives his own reflexions on a conference held in Manchester in January, and points to some of the changes that may have to be made in university science departments to cope with the problem that their size is likely to grow faster than their finances.

MORE teaching, less research, and universities becoming more like schools. That, roughly, is the prospect for the rest of the 1970s that emerged at a conference on problems facing university science organized by the Council for Scientific Policy (CSP) jointly with the Department of Liberal Studies in Science of Manchester University, and held in Manchester in January. Some rather drastic changes in academic science seem inevitable as Britain drags itself painfully into the era of mass higher education—with near-universal higher education on the Californian model as yet barely on the horizon.

Sir Frederick Dainton, chairman of the CSP, prophesied in his opening keynote address that there will have to be closer scrutiny of the real purposes of doing research, of the criteria for allocation of resources to research, and of the connexion between research and teaching. Already, he pointed out, something like £100 million a year is being spent on scientific research in British universities. There is little chance that this amount will grow anything like as fast as the 6 per cent a year increase in student numbers envisaged by the Department of Education and Science, and consequently most of the discussion at the conference was taken up with digesting various implications of the decrease in research intensiveness of the higher education system.

Disillusion

That such a change is inevitable was accepted almost without question. Recognition of public disillusion with science hung gloomily over the conference. It was not only Dr A. A. L. Challis of ICI who took the hardheaded business view that science does not lead easily and painlessly to increase in the gross national product. Other speakers also pointed to the widespread feeling of frustration over the promise of economic prosperity through science, accepted until not so many years ago with what now looks like simple minded faith. So often the modern marvels—the advanced power stations, the hovercraft—just do not work properly. Dainton listed some of the causes and symptoms which have turned the unclouded optimism of the 1950s into the present uncertainty: concern over the environment; the brain drain—now reversed, but more because of a changed situation in the United States than because of any improvement in Britain; the swing away from science in sixth forms; overspecialization at university and a shortage of candidates for traditional courses; unit costs rising in an atmosphere of tightening financial stringency.

When historians come to analyse the attitudes of the early 1970s, will they see all this breast-beating by the scientific community as early signs of a new realism or only as a swing of a pendulum? No doubt it is true that science has in the past been grossly oversold; only the naïve and the uninformed can seriously suppose that it can continue the kind of growth it has enjoyed since the Second World War. But has the time perhaps come when more academics should jump off the self-denigratory bandwagon and recapture some of the old idealism? After all, together with the problems, science has delivered a lot of goods.

Future of Research Councils

One expression of the general feeling that society at large is not getting enough value out of investment in research appears in the rumours now current that some of the research councils might be taken over by the government departments corresponding to their chief interests. The idea would be to bring them closer to the users, so as to make their research strategies more user-oriented. In particular, the Agricultural Research Council is felt to be in danger of being taken over by the Ministry of Agriculture, Fisheries and Food, and Dr N. W. Pirie, of the Rothamsted Experimental Station, spoke of the unsettling effect on the scientists employed there.

As for the Medical Research Council, its secretary, Dr J. A. B. Gray, gave a spirited defence of the present system as against any possible marriage with the Department of Health and Social Security. His reasoning resembled the time honoured objection to monogamy: it was not so much a refusal to form one liaison as a reluctance to cut off all the others. The MRC, he pointed out, does not serve just one user but is the centre of a complex network of contacts, advice and support.

As chairman of the largest of the research councils—the Science Research Council—Sir Brian Flowers is in as good a position as anyone to give an inkling of what closer scrutiny over research funds might eventually mean in practice. The SRC's policy is to concentrate resources so that centres of excellence can be built up and maintained. Perhaps there are overtones of élitism in this approach, but the alternative is to spread resources so thinly that they cannot be effective anywhere. One implication of the policy of selectivity is that not all universities can be equally good at everything; perhaps only a dozen will become recognized as generally strong in science. Already the SRC is choosing fields of science for selective support. At present, however, 80 per cent of the funds for research grants is still being allocated by "passive response" to unsolicited requests, and only 20 per cent to "stimulated applications".

The case for concentration was reinforced by another line of argument put forward by John Ziman, professor of physics at Bristol University, who focused attention on graduate training rather than quality of research. Using order of magnitude calculations, he sought to show that the growth of higher education will so dilute the ratio of research students to university teachers that drastic selectivity will be unavoidable to maintain viable graduate schools in a limited number of centres.

What the crystal ball shows, then, is a hierarchy of institutions in which the differentiations are more, not less, marked than at present. Gone will be the polite pretence of equality of opportunity between universities. To most people it seems politically unacceptable to restrict entry to first degree courses because of assertions of the interdependence between teaching and research. But with how much equanimity can we move into a situation in which a high proportion of teachers for first degree courses will not be engaged on research? What will maintain the quality of their teaching? Will it be enough that once, years ago, they did research? Can they be expected to keep in touch by in-service training and by rubbing shoulders with research workers?

The deeply rooted notion that the quality of teaching can be measured as an inverse function of its distance from the life-infusing light of research may have to be discarded. Belief in the dependence of teaching on research rests more on the frequency of repetition of the assertion than on solid evidence. There are those who point out that research can distract from teaching rather than enliven it. And it may be possible to find alternatives to research of the traditional kind. Engineers say that design and consulting work can also give the mind that liveliness which comes from being at a frontier of knowledge. Those who are oriented to teaching might even dare to suggest educational development work on curricula and teaching methods to act as research-surrogates in the occupational therapy prescribed by custom for academic staff.

Collaboration

"If you can't afford it, share it" was Flowers's prescription for high cost research. The alternative to opting out of expensive fields is to collaborate in them. It was a pity that there was so little discussion at the conference of the sharing of national resources between universities in Britain. A good deal of attention was, however, devoted to the more glamorous forms of collaboration that extend across national boundaries. The special favourite was, of course, the CERN accelerator at Geneva, on which papers were presented by both Dr A. W. Merrison, vice-chancellor of Bristol University, and Dr M. Gibbons of the Department of Liberal Studies in Science at Manchester. No one could have left the conference with any doubts still lingering about the immaculateness of its conception or the excellence of its execution.

There are, however, implications of this kind of research which still do not seem to be fully appreciated by much of the scientific community. In high energy nuclear physics, even the most academic of scientists cannot be free to do experiments "just to see". He accepts, without too much grumbling, that his proposal has to run the gauntlet of a series of committees. It may take three years, if all goes well, to get an allocation of beam time on the big machine. The organization of an experimental run reminded Gibbons "of a production process in industry or the NASA mission control centre at Houston". So what has become of the traditional idea that good research is possible only when the intellect is left free to explore ideas unhindered? In Britain, the national research effort has to be oriented to the international programme. Universities must be willing to release staff to work at the big machine—but this means that links between the research and the educational system become increasingly tenuous.

Problem-orientation

No conference such as this could have gone by without criticizing university courses for being overspecialized. Dr T. M. Sugden, of Shell's Thornton Research Centre, complained that first degree graduates commonly have indigestion and PhDs are liable to suffer from constipation. Varying the metaphor, Sir Robert Cockburn, formerly director of the Royal Aircraft Establishment, Farnborough, judged that it takes an average of three years to "defrost" a university graduate.

The fashionable remedy—laxative or anti-freeze as the case may be—is to swing from discipline-orientation to problem-orientation. Clothed in various vocabularies and contexts, this was a recurrent theme. Professor A. H. Bunting, of Reading University, stressed the "primacy of the problem", with science put in its place as just one of the resources for achieving solutions; from his own field, agriculture, he illustrated this by the marked success of a highly mission-oriented US team in increasing food production in India more in four years than the British did over a much longer time.

Alan Pearson, director of the Research and Development Research Unit of the Manchester Business School, gave a specification of the abilities required of scientists working in industrial environments: to identify problem areas, to handle unstructured problems, to work effectively with other people, and to communicate with non-specialists. But can such qualities be taught? Only, he thought, through project-based courses, the projects preferably being set up jointly with industry, in spite of the expense and difficulty involved. This approach clearly cannot be envisaged for all undergraduates—it could be adopted only on a more select basis, chiefly at postgraduate level.

Listening to criticisms of university science, one begins to feel that it has all turned into a sort of ritual: the practical problem is the totem, specialization is taboo. This is not to say that such criticism is no longer necessary. But perhaps it should now be directed less at the universities, which have already innovated more than many people recognize, than at those schools which continue to send most of their ablest sixth formers to the more traditional courses, ignoring or distrusting the new.

The difficulty with new courses, of course, lies in distinguishing the hasty pot-pourri from the carefully planned and well served meal—it must be admitted that change is not always progress. Courses that look too much outward at real life problems can give the appearance of a Certificate of Secondary Education philosophy extended, far beyond the one extra year provisionally blessed last summer by the Schools Council, into the less appropriate realm of the universities. Academics tend, whether rightly or wrongly, not to recognize such work as suitable preparation for more advanced study, so projects develop into educationally terminal diseases.

Moreover, there are limits to what can be expected from an educational system. Some critics seem to imply that universities are failing to help young people achieve their ambition to do well in industry. The fact is that many of them have no such ambition. Imbued with vague anti-materialist sentiments, they often fail to crystallize these sentiments into any specific activity, such as teaching in an underdeveloped country, and this is what so exasperates the careers adviser. But can a university teach students to want money more urgently? And if it could, should it?

More Open Politics ?

An intriguing aspect of the conference was the sprinkling of younger scientists mixing with the "establishment" men; not that they made much impact, outnumbered as they were. Most of the talking was done by "that self-congratulatory group who have got out of the system all they want", as Flowers put it. Nevertheless, there was a feeling that a conference such as this could not have happened even a few years ago. The politics of British science has hitherto been a very closed affair. However rosily the SRC might be described as "a forum of the scientific community", to most practising scientists it has seemed, like all the science policy bodies, more like an outpost of inscrutable officialdom. Are the policy makers now moving to more open, more "democratic" decision-taking, so as to counter accusations that they are a faceless gerontocracy of committee men meeting behind closed doors?

If so, they could have a long way to go. They might have to do more than include a few lecturers among the professors on the carefully constructed invitation lists. Can we envisage faculties sending elected representatives of non-professorial staff to future meetings? Or even students? It seems an unlikely prospect. With policy so firmly set to sacrifice equality to quality, it is hard to imagine the political structure moving far in the opposite direction.

Defence of the Berkeley Work on Alpha-emitting Isotopes of Element 104

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In the past two years, there has been some controversy about conflicting claims of Russian and American scientists to have demonstrated the formation of isotopes of Element 104 by nuclear reactions induced by high energy particles. This article is a restatement of the American case by Professor A. Ghiorso's group at Berkeley.

CERTAIN questions have been raised regarding the validity of our work[1] on the discovery of two alpha-emitting isotopes of element 104 (rutherfordium). Doubt was first expressed by V. A. Druin at the international conference on nuclear reactions induced by heavy ions[2] at Heidelberg, Germany, in July 1969. These doubts were repeated in a paper submitted to *Yadernaya Fizika*[3] in November 1969 by Akapiev *et al.* In this same month the Robert A. Welch Foundation Conference on Transuranium Elements—the Mendeleev Centennial was held at Houston, Texas, and the issues were discussed at length after the presentation of papers[4] by A. Ghiorso and by I. Zvara. Apparently this discussion did not sufficiently clarify the matter because strong doubts were again published in *Atomnaya Energiya* by G. N. Flerov[5].

In our article[6] on the discovery of an alpha-emitting isotope of element 105 (hahnium), we carefully included answers to the major criticisms, but in view of the continued charges made by the Dubna group we feel that a detailed rebuttal is in order. We shall attempt here to perform this function and in addition will present new evidence in support of our original work.

The research on the heavy element alpha-emitters is fraught with the hazards of low production cross sections which lead to numerous possibilities of misidentifications because of the presence of background activities with similar alpha energies and half-lives. Having pioneered in this field we are aware of these problems and have devoted much of our efforts to determining and eradicating sources of troubles. We feel that we have been conservative in our published claims and are thus much surprised by some of the criticisms levelled at our work. Perhaps we have misjudged the necessity of including a very detailed discussion of possible background effects.

A review of the general methods used in these experiments will help to clarify the discussion of our results. The basic technique takes advantage of the large forward recoil imparted in a heavy ion reaction to separate the transmuted atoms from the usually highly radioactive target. In order to provide a very thin sample for alpha particle energy analysis, the recoiling atoms are stopped in helium gas at a pressure of 500–1,000 torr and then allowed to escape with the gas through a small orifice into a rough vacuum where they impinge and stick on the rim of a 50 cm diameter wheel. The wheel acts as a conveyor and periodically carries these deposited atoms to positions adjacent to solid state silicon alpha detectors for energy analysis. Half-life information is obtained from the relative numbers of alpha particles observed at each detecting station and also from the decay observed at each station while the wheel is stationary. The data are stored by a PDP-9 computer and ancillary equipment.

In favourable cases, it is possible to determine the mass and atomic number of the nuclide being studied by identifying the daughter nucleus which recoils from the rim of the wheel as the result of alpha particle decay of its mother. To make this measurement possible, the detectors which have been adjacent to the wheel are shuttled about 2 cm to positions opposite similar detectors at suitable intervals so that they can be examined at high geometry for the daughter activity. In our first published experiments on element 104, we used four mother and four corresponding daughter detectors. Later, to recover the time lost while the mother detectors were shuttled off the wheel, the detector system was duplicated so that the mother and daughter measurements could be made simultaneously. Thus, at each station four detectors were installed, two shuttled and two unshuttled. The number of detecting stations was first increased to five and finally to seven so that our present system makes use of $7\times4=28$ detecting crystals (Fig. 1).

We now take up the criticisms raised by Akapiev *et al.*[3]. We will first present what we believe to be a fair statement of the major charges raised by that report and then follow it with our answer. To help the reader follow the arguments, we have reproduced two figures (Figs. 2 and 3) along with their captions from the original publication.

The Berkeley group did not present alpha spectra of background activities that would be produced by the bombardment of lead impurities with carbon ions and did not discuss any background effects

These statements are both true. Because of the stringent word and figure limitations set by *Physical Review Letters*, there was no detailed discussion of this aspect of the experiments. We did, however, carefully state that we had made bombardments with other ions and thus implied that suitable background checks had been made. The fact that certain Pb-produced peaks in the alpha spectra such as ^{214}Ra and ^{209,210,212}Rn were labelled also implies that we were clearly aware of background effects caused by a lead impurity. The simple fact is that the element 104 alpha activities were so clearly above the backgrounds usually encountered that this problem was almost irrelevant. Thus we devoted the space available to other important phases of the experiment.

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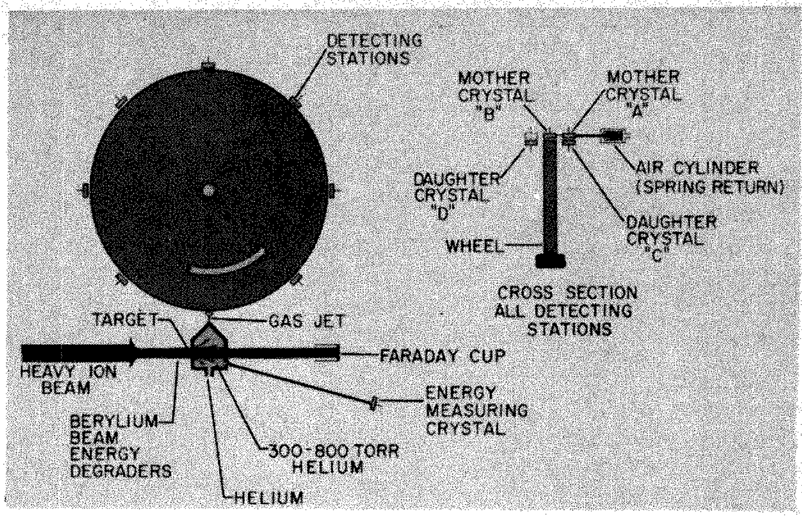

Fig. 1 A schematic representation of the vertical wheel system with seven detecting stations. On the right hand side a cross-section of one of the detector stations is shown.

Well known Pb-produced nuclides do not decay with their proper half-lives, e.g., 30 min ^{209}Rn and 2.7 h ^{210}Rn

The main activity in the 6.043 MeV labelled peak is due to ^{210}Rn and arises as the alpha-recoil daughter of 2.6 s ^{214}Ra which is produced from a tiny lead impurity in our californium target. Since the Rn isotopes will not stick to the wheel as they emerge from the gas jet (this can only happen if the collecting surface is cooled to a very low temperature), they can only appear in the spectra either by being detected as gaseous atoms in the wheel housing or by being embedded into the detector surfaces by nuclear recoil. As we shall show, the former condition does not prevail. But in the latter case, the Rn isotopes would appear to have the half-life of the mother atoms since the amount deposited into each detector face would depend on the wheel-cycle period. If the half-life is measured by the relative amounts of activity seen by each detector, the mother half-life would determine its value, but if the decay at each detector is monitored, the half-life of the daughter would be measured. Thus it was that the 6.043 MeV peak appeared to decay in the successive alpha spectra with a 2.6 s half-life since it was controlled by ^{214}Ra. There must have been some ^{209}Rn (which has the same alpha energy) present in this peak since it is produced as the daughter of 2.75 min ^{213}Ra, but it was a minor component.

The alpha particle peak at 8.87 MeV can only be due to the 25 s ^{211m}Po and thus cannot decay with a 3 s period

We were very careful to point out that the origin of the 8.87 MeV peak was uncertain and we did not claim that it was due to ^{257}104. From recent results, we find that several sources can contribute to this peak in the alpha spectra.

(*a*) One obvious source, it is true, is 25 s ^{211m}Po, as demonstrated in Fig. 5, where a lead target with some 50,000 ng cm^{-2} has been substituted for the ^{249}Cf target which contains about ng cm^{-2} Pb impurity. The polonium activity has a 25 s half-life both as measured from the relative amounts of activity observed at each station and by the decay while the crystals are stationary.

(*b*) When our work[1] was published, we were unable to assign the short lived component in the 8.87 MeV peak to any known nucleus, as was pointed out in the figure caption (Fig. 2). Not until we started working on element 105 did we accumulate conclusive evidence that ^{257}Lr has a half-life of 0.7 s and also a most prominent alpha group at 8.87 MeV, as opposed to the Dubna group's[7] claim that it has a half-life of 35 s and an alpha energy of 8.5–8.6 MeV. By resolving the 8.87 MeV peak of the repeat experiment (to be discussed later) into two components we find that about one half of the activity is due to 0.7 s ^{257}Lr and the other half to 25 s ^{211m}Po.

(*c*) It is conceivable that 5 s ^{257}104 can have a weak alpha group at this energy but this cannot be resolved easily because of the interfering activities.

All Berkeley half-lives in the heavy element region must be questioned because the apparent half-life of 30 min 7.43 MeV ^{250}Fm is obviously only a few seconds

For some time, the strange phenomenon associated with the peak at 7.43 MeV troubled us greatly. We at first quite naturally assumed that the apparent short half-life of about 2 s was a real measure of the half-life of this peak and so thought it might be due to 0.5 s ^{211}Po, which has this energy, plus some longer lived background. We finally discovered

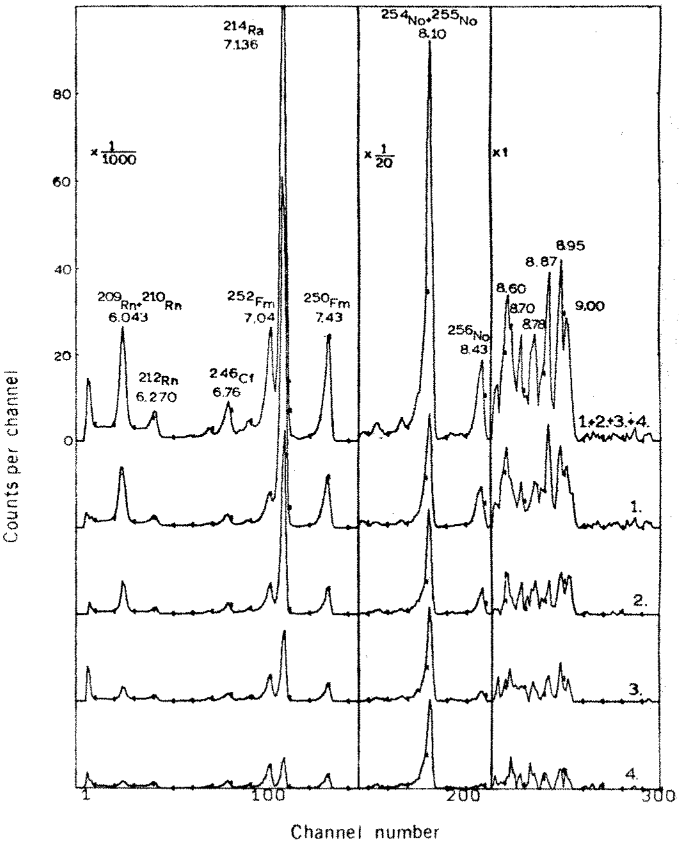

Fig. 2 "A series of alpha spectra of the activities produced by bombardment of ^{249}Cf with 71 MeV ^{12}C ions. The top spectrum is the sum of the individual spectra from the four detectors. The 8.60 MeV peak is probably due to ^{258}Lr; the peaks above that energy belong to ^{257}104 with the exception of the one at 8.87 MeV whose origin is uncertain[1]". (See text: this peak is now known to be due to ^{257}Lr and ^{211m}Po.)

that the peak persisted after bombardment ended and decayed with a 30 min half-life at each detector even when the wheel was removed. Further, it was found that the ^{246}Cf daughter of ^{250}Fm was also observed in each crystal and corresponded roughly to the amount of its parent. It was obvious then that the activity was ^{250}Fm which had been transferred to the face of each crystal, and the question became that of knowing how the atoms lodged there. They could not have been transferred as the result of alpha recoil from ^{254}No for two reasons: first, the number of atoms required was far in excess of that observed and, second, half-life is well known to be 55 s[8,9].

Over a period of time we have made additional observations and experiments so that now we can offer the following explanation which appears reasonable. We have found that another isotope of fermium, ^{252}Fm, which was made in good yield at the same time as ^{250}Fm, was not transferred. We also found that ^{254}No was transferred to the detectors with a 0.2 s apparent half-life, even though another isotope of nobelium, ^{255}No, was not. We also looked with high sensitivity but without success for the transfer of the prominent activities ^{214}Ra and ^{213}Fr. We decided that the movement of atoms from wheel to detector was not a mechanical or chemical effect but must be due to the recoil afforded by transitions from isomeric states in the two nuclides, ^{250}Fm and ^{254}No. To prove that this was the case, we biased the wheel negatively by 10 V relative to the crystals and increased the gas pressure in this region to 5–10 torr. By this technique we were able to reduce the transfer of these activities by an order of magnitude.

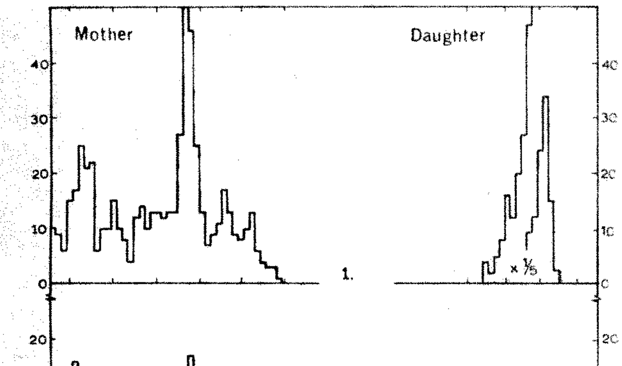

Fig. 3 "A set of spectra from the mother–daughter experiment which demonstrates the genetic relationship between ^{257}104 and ^{253}No. The spectra recorded by the individual crystal pairs are shown on top with the sum of the last three pairs at the bottom[1]".

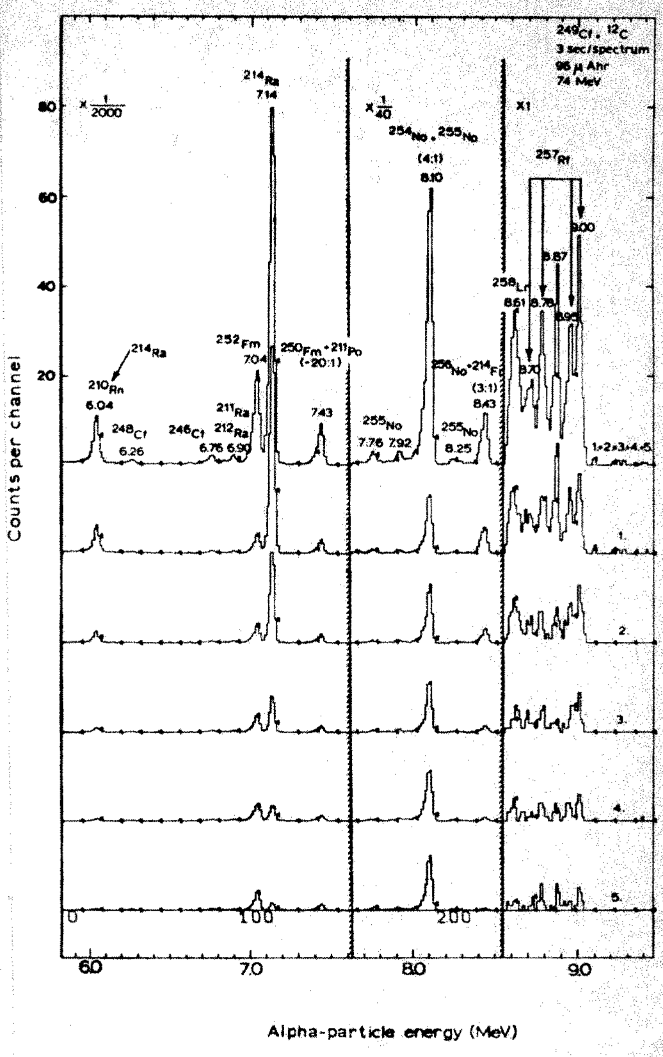

Fig. 4 A series of alpha particle spectra of the activities produced in repeat experiments when bombarding the ^{249}Cf target with 74 MeV ^{12}C ions. A 20 detector system was used instead of the 8 detector one used in the experiments resulting in the spectra shown in Fig. 2. The wheel cycle rate was 3 s in both series of experiments.

A very strong corroboration was furnished by the bombardment of ^{242}Pu by ^{12}C ions. At 72 MeV, which is near the peak of the (^{12}C,4n) reaction, the transfer of 30 min ^{250}Fm was observed with the same apparent half-life as in the carbon ion bombardment of ^{249}Cf. This experiment rules out the rather remote possibility that a 2 s ^{250}Md, decaying by electron-capture, can be the source of the transfer of ^{250}Fm since elements with atomic number greater than 100 cannot be made in this bombardment. It is also extremely unlikely that a 2 s beta-decaying isomer of ^{250}Es can be responsible. We can only conclude that an isomer exists in ^{250}Fm itself and a final test which is to be conducted will be with the reaction ^{249}Cf(He^4, 3n)^{250}Fm. A full report on this very interesting nuclide will be published later.

With only the evidence afforded by this unusual transfer phenomenon, the Dubna group suggested that all of our half-life measurements could be in error because of some undiscovered artefact of our system. Suffice it to say that we have obtained the same values for many nuclides as they have and most of these half-lives were measured before their published work. These measurements vary in range from 3.2 s[9] for ^{256}No (which from 1963 to 1967 was quoted as 8 s by its Russian discoverers[10]) to 200 s[11] for ^{255}No.

Apart from statistical considerations, we have found no reason to doubt our decay periods.

The construction and geometry of our set-up cause "3 s" to be a characteristic value in our measurements. In particular, activity may be collected directly on the detector faces by gas-jet leakage around the wheel

To determine whether a small amount of activity could bypass the wheel and be collected on the detector faces, we have performed an experiment to measure such an effect. In our normal conditions, some 2×10^6 alpha counts of ^{214}Ra were observed from carbon ion bombardment of a lead target with the wheel being cycled at a rate of 3 s per detecting station. The wheel was then stopped and the measurement repeated for an identical integrated beam charge. Not one count which could be ascribed to ^{214}Ra was observed in any of the detectors. This was not particularly surprising to us since the volume through which the wheel is rotated is carefully shielded internally by lead sheets to reduce the fast-neutron degradation damage of the silicone detectors. We feel we can state categorically that in our system there is no significant direct transfer by a gas leakage path. Our "3 s half-lives" can only be the result of nuclear characteristics beyond our control.

The half-lives of ^{257}104 and ^{259}104 could be much shorter because there is an excess of ^{253}No and ^{255}No on the first detector

This criticism must be answered in two ways. (*a*) If there were such an excess of these two isotopes on the first detector, then why would not the alpha particles from their presumed parents be also observed in this same detector? (*b*) We never said that there was an excess of either ^{253}No or ^{255}No in the first detector. The excess activity was identified as ^{254}No (from its decay on the detector with a 55±20 s half-life). We used this isotope of nobelium as a monitor of the amount of "self-transfer" in the daughter measuring experiment. It now seems that this transfer was accomplished by the decay of the ^{254m}No I.T. with a 0.2 s half-life as we have explained.

The Berkeley experiment can be compared with a background run made at Dubna with a lead plus carbon ion bombardment which shows an overwhelming ratio of ^{211m}Po to ^{214}Ra

The Russian experiment is by no means a suitable substitute for our experiments on element 104. They used a lead target weighing 1,500 μg cm^{-2}; we used a californium oxide target weighing about 300 μg^{-2}. They used a mixture of helium and nitrogen gases in their recoil chamber; we used only helium. The recoil chamber dimensions and gas pressure are not given but we suspect that they must be using one much larger than ours at a higher pressure and thus capable of stopping more noncompound-nucleus recoils. It has been our experience that the yield of ^{211m}Po depends critically on these parameters and on other factors such as the impurity content of the carrier gas—even beam level can play an important role. Our experiment has been carefully tailored to maximize the heavy nuclide yield and reduce that of interfering activities, and so it should not be too surprising if our ratio of ^{211m}Po to ^{214}Ra is lower than in their experiment. We do know that there is some ^{211m}Po in the 8.87 MeV peak, but it has not affected the interpretation of the nearby alpha groups which belong to ^{257}104. It is clear that the Dubna system operates differently from ours because of the large amount of ^{213}Rn (8.09 MeV peak) visible in their spectrum. It seems to us that this can be observed only by decay from gaseous atoms of radon in the vicinity of the detectors since the amount is hundreds of times larger than that which could come via electron-capture branching from the 6.77 MeV ^{213}Fr, no trace of which is visible in the Russian spectrum.

These criticisms and their rebuttals we believe to be a fair summary of the arguments levelled at our experiments. A more satisfying answer, perhaps, is furnished by what follows. We have repeated the ^{249}Cf(^{12}C,4n)^{257}104→^{253}No experiment with a higher efficiency and better resolution. A background experiment was also performed with a 50 μg cm^{-2} lead target. This was not exactly a substitute for the californium experiment, serving only as a reasonable approximation, but it did show that ^{211m}Po was not an important problem. The new experiment on element 104 gave statistically better information than the previous run even though it was completed in a shorter time.

The results of the repeat experiments are presented in Figs. 4, 5 and 6. The first one displays a series of alpha particle spectra of the activities produced in bombardments of the ^{249}Cf target with 74 MeV ^{12}C ions. The experiment was carried out with the 20-detector system and the spectra shown are from the detectors in the on-wheel position. The wheel-cycle rate was 3 s per detecting station. The activities assigned to isotopes of Ra, Fr, Rn and Po are due to a lead impurity in the target. A small amount of mercury contaminant in the material backing the target does not significantly add to these activities. Where two activities contribute to the same peak, the approximate ratio of the two is shown below the peak label. It should be noted that the 6.26 MeV peak is predominantly due to ^{248}Cf, not ^{212}Rn (Fig. 2). The 6.04 MeV ^{210}Rn peak has the apparent half-life of its mother, ^{214}Ra, because the observed events are mostly due to the decay of ^{210}Rn atoms recoiled into the detectors as a result of the alpha decay of ^{214}Ra atoms.

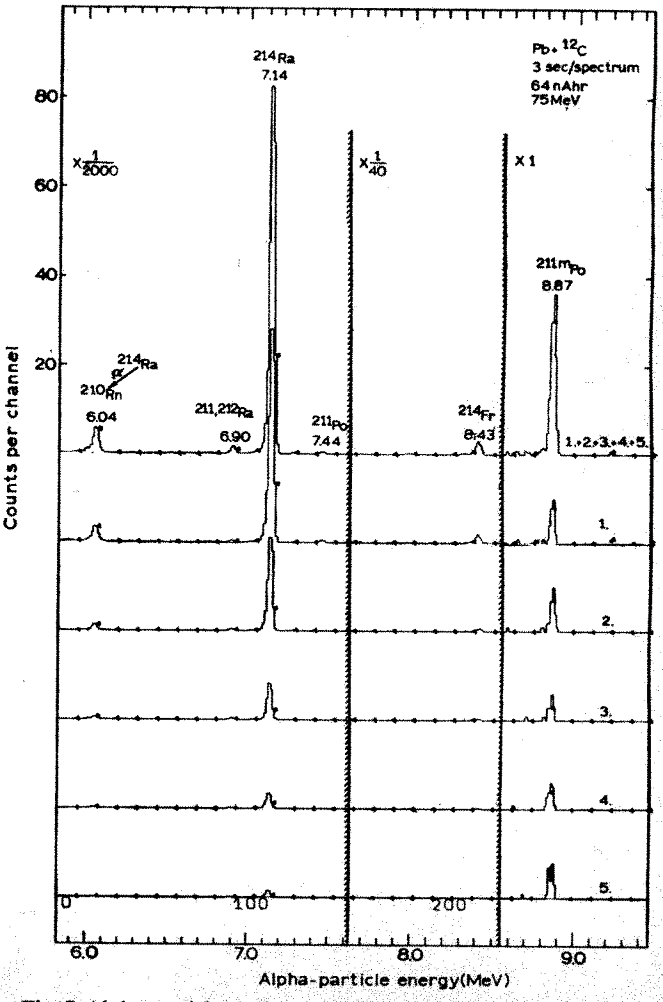

Fig. 5 Alpha particle spectra resulting from an experiment where the ^{249}Cf target was replaced by a lead target.

The peak at 8.87 MeV results from the decay of ^{257}Lr and ^{211m}Po, both of which contribute about equal amounts. The assignments of the 0.7 s component to ^{257}Lr was confirmed in connexion with the experiments on element 105 by a cross-bombardment utilizing the ^{249}Cf(B^{11},3n)^{257}Lr reaction.

Fig. 5 displays a series of alpha particle spectra of the activities produced in bombardment of a natural lead target by ^{12}C ions under similar conditions to those in Fig. 4. The ratio of ^{210}Rn/^{214}Ra is smaller than in Fig. 4 because the decay of ^{210}Rn was not followed equally long after the bombardment. Because of the differences in target thicknesses and beam intensities, and the difference of about 1.5 MeV in the bombarding energy of the ^{12}C ions, the ratio of ^{211m}Po(8.87 MeV)/^{214}Ra(7.14 MeV) is greater by a factor of two in the lead spectrum.

The series of alpha spectra from the same experiment as in Fig. 4, but recorded by the crystals in the off-wheel position, is shown in Fig. 6. The on-wheel–off-wheel cycle, or shuttle period, was 100 s, while the wheel-cycle rate was 3 s. The presence of ^{250}Fm and ^{254}No alpha particle peaks with apparent half-lives of 2 s and 0.2 s, respectively, is believed to be caused by isomeric states of these isotopes, as previously explained. The other peaks in the spectrum are caused by the decay of alpha-recoil atoms on the movable detectors.

The apparent half-life of ^{253}No obtained by measuring the amount of ^{253}No recoiling at each detector station is 4.4 ± 1.0 s. This is in agreement with the value 4.8 ± 0.5 s for ^{257}104 as measured directly by the amount of activity observed at each station. Summing the detected daughter events by the four 25 s time subgroups of the 100 s shuttle period, one obtains a half-life of 90 ± 30 s for the 8.01 MeV alpha particle group which is consistent with the 105 s half-life[9] of ^{253}No. The ratio of counts in the alpha particle peaks assigned to ^{257}104 to those in the 8.01 MeV peak in Fig. 6 is 506 : 137 or 3.5. A calculation taking into account geometry and timing conditions gives a value 2.5. This difference could possibly be an indication of some 20–30% electron capture branching in the decay of ^{253}No.

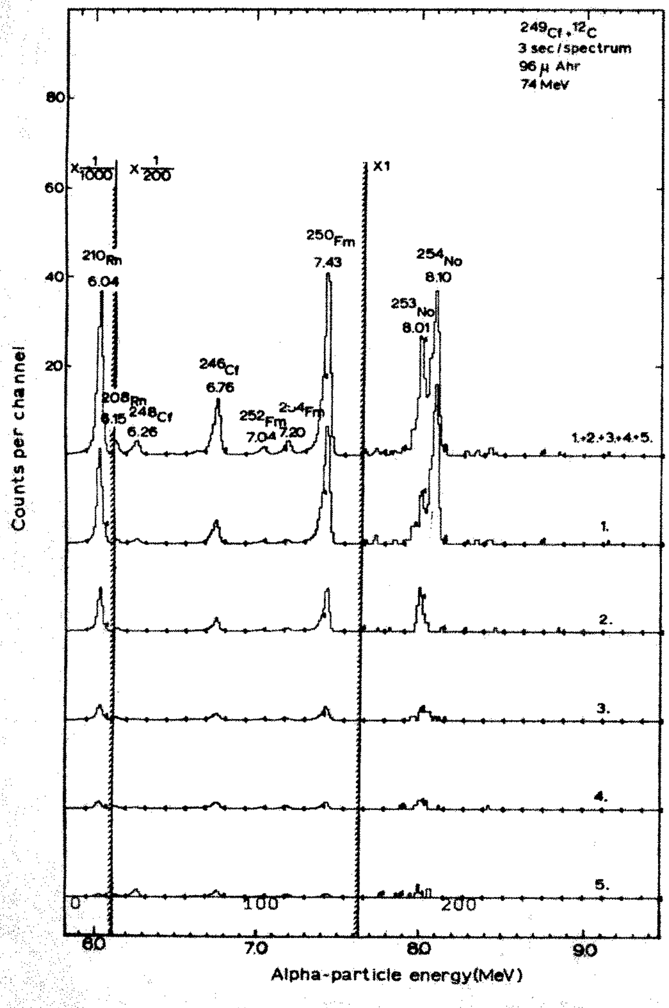

Fig. 6 A series of alpha particle spectra from the same experiments as in Fig. 4 but recorded by the crystals in off-wheel position. These spectra correspond to those displayed in Fig. 3, but show a wider range of alpha particle energies.

The same equipment has been used to discover another isotope of rutherfordium. This work[12] characterized the 65 s alpha emitter, ^{261}Rf, and showed conclusively that its 26 s daughter, ^{257}No, was observed as the result of alpha particle recoil-transfer from its mother. This discovery was confirmed chemically when it was shown[13] by fast aqueous chemistry experiments utilizing this isotope that rutherfordium was a trans-actinide element. More recently, this system has been used in the discovery[6] of an alpha-emitting isotope of element 105, the 1.6 s ^{260}Ha. The fact that the radiations detected in these two sets of experiments were completely different shows that there is no built-in constant background effect that could conceivably mislead us in our interpretations of other results.

In conclusion, we feel that we can safely draw the following conclusions: (1) The additional experiments with ^{257}Rf which have been described above fully confirm our original findings. (2) The puzzling transfer phenomenon has been explained as the result of previously unknown isomeric transitions in the even–even nuclides, ^{250}Fm and ^{254}No. (3) The unknown 0.7 s and 8.87 MeV activity has been determined to be due to ^{257}Lr. (4) There is no gas leakage in our system that can transfer activity directly to the detector faces. (5) Our system does not have a "characteristic half-life due to some unexplained artefact".

In our opinion the performance and reliability of our experimental system are beyond reproach. The present multidetector shuttle apparatus is quite a complicated instrument which has required a great deal of development and testing, and its value as a research tool has been proved by the quality of the nuclear spectroscopic data obtained for the seven isotopes of nobelium, five of lawrencium, three of rutherfordium, and one of hahnium which have been characterized up to the present time.

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Ageing of Mammals

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In his theory of ageing Professor Bullough suggests that in mammals it is stress which delays cell death through its effect on the chalone mechanism.

THE phenomenon of ageing and death presents a biological problem of the greatest interest and importance[1–4]. The most basic question is whether ageing is an inherent feature of all cells and organisms. If it is, then a long life must be regarded as the mere postponement of inevitable death; if it is not, then a limited life span must be something which has been superimposed, presumably because it confers some benefit on the species. It seems that this second alternative is to be preferred, and indeed Weismann[5], in 1891, concluded that death, wherever it is found, "can be very well explained as a secondarily acquired adaptation". Certainly most protozoans or many lower metazoans "fail to show ageing . . . because of a continual replacement regimen" and so they have an "indeterminate" life span[2].

According to Comfort[6], senescence depends essentially on "a cellular information loss, probably in fixed cells, and originally at the molecular level". The theories on information loss fall into two groups, which are not necessarily exclusive. The first holds that ageing is due to the steady accumulation of random and permanent forms of cell damage leading to reduced function or to malfunction in one or more vital tissues. The second holds that ageing is basically directed by some inbuilt control mechanism. According to Medawar[7] and Williams[8] this mechanism may depend on the actions of "pleiotropic genes", which are advantageous in a young animal at the expense of their becoming disadvantageous later in life. However, such genes remain hypothetical, and Sacher[9] has trenchantly concluded that although "physically possible" they are "absurdly unlikely".

A more tenable viewpoint emphasizes the potential importance of a mechanism of ageing which is not hypothetical and which is controlled by genes that continue to act in the same way throughout life[4]. This mechanism, which is basic to tissue organization, is already known to determine the life span of cells of many mammalian tissues, and at least in theory it could readily be adapted to determine the life span of the animal itself. It is this theory that is examined here.

Tissue Organization: Cell Gain

The key to the mortality of mammals certainly lies in their tissues, which although superficially diverse are all organized to the same plan. Each tissue and each organ must be maintained at a mass which is appropriate to the total body mass; this is a problem of cellular homeostasis.

Cellular homeostasis is based on mitotic control. In theory it is possible to envisage the creation of an animal by mitosis and differentiation and then the survival of that animal through an adult life in which no further mitosis or differentiation occurs. Such a situation may exist in many adult insects and it is certainly found in the non-mitotic neural and muscular tissues of mammals. However, most mammalian tissues retain a mitotic potential which is invaluable for the repair of damage.

In all tissues examined so far the method of mitotic control is essentially the same: the rate of production of new cells is determined from moment to moment by a negative feedback system[4]. The tissues already studied from this point of view are epidermis[10], sebaceous glands[11], melanocytes[12], lung alveoli[13], kidney[14,15], liver[14], granulocytes[16], erythrocytes[16], and lymphocytes (unpublished results of E. B. Laurence and myself); in all these cases the cells synthesize a tissue-specific antimitotic messenger molecule, called a chalone, which limits the rate of cell production (Fig. 1, point A). Chalone control systems may be present in all mammalian tissues, although in some tissues other control systems, which are commonly hormonal, may be superimposed[4].

Of particular interest has been the discovery that the antimitotic power of most of the known chalones is strengthened by the presence of the two stress hormones (adrenaline and a glucocorticoid hormone). It is this which gives rise to the well known diurnal mitotic cycle[17]: with low stress hormone output during sleep the mitotic rate rises and with increased stress hormone output on waking the mitotic rate falls. This mechanism may have little practical significance in normal circumstances but in the wild it may act in stressful situations, especially during long periods of hunger, to reduce the metabolic demand of an unnecessarily high rate of cell production.

All mitotic tissues contain two basic cell types: those which are involved in the mitotic cycle and those which are post-mitotic and which are passing along the ageing pathway to their death (Fig. 1). Thus each tissue is in a state of flow and it is the post-mitotic ageing cells that are responsible for tissue function.

Any cell entering the ageing pathway has a particular life expectancy that is typical of that tissue. It is well known that the higher the mitotic rate the shorter this life expectancy: in epidermis with a moderate mitotic rate the post-mitotic life span is 14–21 days[18,19], while in duodenal mucosa with a high mitotic rate the life span is only about 2 days[4]. These tissue characteristics, however, are not inflexible. If in any tissue the mitotic rate increases, so too does the rate of ageing of the post-mitotic cells; thus in epidermis with chronic irritation or psoriasis the life span of the post-mitotic cells is reduced to 4–5 days[18,19]. Conversely if the mitotic rate falls, as in epidermis and sebaceous glands during continued stress, the rate of post-mitotic cell ageing is also reduced[20]. These changes in the cellular life span ensure that the tissue neither becomes too gross (perhaps even to the point of tumour formation) nor shrinks to the point at which the life of the organism is endangered.

They also show clearly that a post-mitotic cell does not normally die because it is worn out but that its time of death is dictated, according to circumstances of the moment, by the same physiological mechanism that controls the mitotic rate.

In a mammal the neurones and the skeletal and cardiac muscles are established by mitosis early in life, especially during the embryonic and foetal stages. At some time shortly after birth the mitotic genes are switched off and thereafter growth in tissue mass is achieved by growth in cell size. By the same means the adult skeletal and cardiac muscles can temporarily increase in mass to meet a temporary increase in metabolic demand, and a similar response is also possible in the cells of some mitotic tissues.

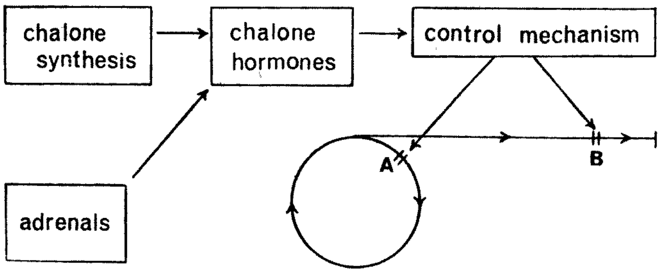

Fig. 1 Diagram of the chalone control mechanism in a typical mitotic tissue such as epidermis. Chalone action is strengthened in the presence of the two stress hormones from the adrenals. An inhibition of mitosis at point A is accompanied by an inhibition of cell ageing at point B.

The situation in a typical non-mitotic tissue is shown in Fig. 2 (compare Fig. 1). Although the mitotic genes are inactivated, the other half of the normal pattern of tissue organization, the ageing pathway, is apparently still functioning. It has already been noted that a reduction in mitotic activity is accompanied by a prolongation of the ageing pathway, and it is obviously to be expected that in non-mitotic tissues this pathway will be particularly long. This is certainly true in neurones and in the skeletal and cardiac muscles, but although the inhibition (Fig. 2, point B) preventing cell death is powerful, it seems that it may not be absolute and that the loss of cells may continue throughout adult life[21]. It has been suggested that in the adult human brain some 10,000 neurones pass this point to die every day[22], and even if this figure is grossly inaccurate the principle evidently holds. In an old mammal the reduction in brain size, as well as in skeletal and cardiac muscle mass, seems obvious, but much further study is needed especially since contrary evidence has been published[23].

Ageing of Organisms

The search for the basic mechanism which ensures the mortality of the mammals has involved both the mitotic and the non-mitotic tissues.

Regarding the mitotic tissues the most important evidence comes from Hayflick[24], who has found from experiments *in vitro* that while fibroblasts from human embryonic lungs are capable of fifty to sixty doublings, those from adult lungs are only capable of twenty to twenty-five doublings. He has consequently concluded that the cells of mitotic tissues have only a limited mitotic potential and that this may be an important factor limiting the life span of a mammal. But there is still considerable doubt whether these *in vitro* results can be directly related to conditions *in vivo*, and I[4] have noted that "if there is indeed a limit to the mitotic potentiality of an adult tissue it is probable that this far exceeds the normal life span of the animal".

Although Hayflick's theory needs further consideration, and although there may be other important features of the mitotic tissues not yet recognized, at the moment it seems more profitable to search for an ageing mechanism in the non-mitotic tissues. The first problem is why the neurones and the skeletal and cardiac muscles are non-mitotic; by contrast, the smooth muscles, for example of the uterus, remain mitotic. The organization of the non-mitotic tissues is so obviously similar to that of the typical mitotic tissue that it can readily be believed that this condition is secondary. It may also readily be believed that their mitotic potential has been lost because of some advantage that this change confers, and the most obvious possible advantage is, through their decreasing efficiency, to set a limit to the life span of their owners.

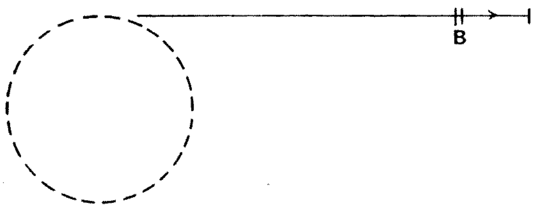

Fig. 2 Diagram of the situation in a typical non-mitotic tissue. With mitosis permanently blocked all the cells pass very slowly along the ageing pathway to their death. It is suggested that point B of the chalone mechanism (see Fig. 1) remains operative.

On this theory it could be the rate at which the non-mitotic cells pass through the point of inhibition (Fig. 2, point B) on the ageing pathway that determines whether life is short as in a mouse or long as in a man. It is not known whether a chalone mechanism exists, in whole or in part, in any non-mitotic tissue. If such mechanisms do exist, however, one test of this theory of ageing would be to discover whether by weakening or strengthening the chalone action it is possible to shorten or lengthen the life span. From what is now known, the easiest way to strengthen the chalone action is to ensure a continuing high level of stress hormone secretion.

The first experiments showing that strengthened chalone action prolongs the life span of the post-mitotic cells were those on epidermis and sebaceous glands[20]. Mice were subjected for many weeks to the stress of a restricted diet, which, however, was adequate to maintain full health. The result was a great enlargement of the adrenal glands and a strong inhibition of epidermal and sebaceous gland mitosis, but since neither the thickness of the epidermis nor the size of the sebaceous glands underwent any significant change it was clear that in both tissues the reduction in cell gain had been matched by a reduction in cell loss.

On the assumption that the inhibition of post-mitotic cell loss is similarly controlled in a non-mitotic tissue, it may be predicted that the rate of loss of the neurones and of the muscle cells should be reduced by any similar form of continued stress. The nervous and muscular systems should then function better for a longer period of time, the life span of the animals should be prolonged, and in particular the condition of the animals should remain relatively youthful. Experiments of this type have been performed repeatedly, though usually for other reasons, and the effects have been dramatic.

The most extensive of these experiments, using several strains of mice, were begun in 1940 by Tannenbaum and Silverstone[25] to test the effects of caloric restriction on tumour incidence. With a carefully restricted diet, tumour incidence fell to a low level even in high cancer strains, but more important it was also found that the dieting mice enjoyed an average life span which was 50–100% longer than that of the normal, fully fed, non-cancer-bearing controls[25]. It was also clear that in their non-mitotic tissues there was a reduction in the rate of metabolic deterioration. This was indicated by the fact that the dieting mice remained sleek and in excellent health with active nervous and muscular systems, while the fully fed controls became senile with weak and shrunken bodies.

In this and many similar experiments subsequently carried out it was assumed that these effects were the outcome of the caloric restriction *per se*. Tannenbaum and Silverstone noted, however, that the adrenals of the dieting mice were greatly enlarged[27] and it has come to seem increasingly probable that both the inhibition of cancer[4] and the promotion of longevity were the outcome of increased adrenal activity. The hungry mice lost sleep because of their continuing and stressful search for food, and in their mitotic tissues there was a reduction of both cell gain and cell loss[20].

If this interpretation is correct then clearly it should be possible to obtain the same effects by prolonged treatment with the stress hormones. Experiments involving adrenaline have yet to be devised (one obvious difficulty is the short life of this molecule in the circulation), but experiments with glucocorticoid hormones have been carried out, for example by Friedman *et al.*[26] and Bellamy[27].

Friedman *et al.* began with the theory that a disturbance of the salt and water balance is an important aspect of old age, and they tested the effects of the continued treatment of 24–27 month old rats with mineralocorticoid and with glucocorticoid hormones. They found that aldosterone, the mineralocorticoid used, was badly tolerated, but that cortisol, the glucocorticoid used, prolonged the life span. They also noted that the glucocorticoid-treated rats maintained better muscle tone and better condition than did the controls.

The results obtained by Bellamy[27] were even more striking, since he began the treatment of his mice immediately after weaning at 3 weeks of age. The mice used were an inbred strain with an average life expectancy of only about 1 year, and they were given a corticosteroid hormone, prednisolone phosphate, in their drinking water. The result was to increase the life expectancy to an average of about 2 years, a response similar in magnitude to that obtained by Tannenbaum and Silverstone. Again the treated mice remained in excellent condition due to the reduced "rate of appearance of age-dependent characters".

All these observations support my theory but none of them is sufficiently conclusive; they could, for example, also be used to support Walford's theory[28] that ageing is basically an autoimmune phenomenon. But they do indicate an invaluable experimental approach to the problem of ageing in mammals. They should now be repeated and elaborated, and particular attention should be paid to the rate of neurone loss from the ganglia (the brain may be too large for accurate measurement) and to the state of the skeletal and cardiac muscles.

Role of Tissues

In mammals, it is well known that whenever the activities of a number of diverse tissues need to be accurately coordinated (as during an annual breeding season), it is usual for only one tissue to act as the initiator and pacemaker. In the case of ageing this would seem to be especially necessary, and if ageing is dictated by the steadily deteriorating efficiency of the non-mitotic tissues then it seems probable that one of these tissues plays the leading role. On present evidence, which is admittedly inadequate, this might be the nervous tissue, and in this connexion it is interesting how Sacher[9] has stressed that in mammals the mass of the brain and the length of life are directly related. Certainly it is known that nervous deterioration leads to muscular deterioration and that this in turn leads to a deterioration of the circulation with repercussions so widespread as to involve all the tissues and processes of the body.

In considering senescence it is necessary to distinguish between "natural" and "unnatural" forms of death. If an animal is enabled artificially to survive into middle and old age, the natural process of ageing is seen in an increasingly exaggerated form, but simultaneously there is an increasing liability to death from a variety of pathological conditions which are unnatural in the sense that they are rarely seen in the wild. These conditions commonly arise from cell damage which can lead to tissue malfunction, to autoimmune reactions[28] or to local unrestrained and lethal tissue growth[4].

At first sight the accumulation of such damage in middle age may seem to be randomly due to extrinsic influences such as chemicals, radiation and viruses, or to intrinsic faults, for example, in gene replication. But this idea of the accumulation of random damage requires some qualification. A house mouse in the second part of a life span of only 2 years is as liable to die from such pathological changes as is a man in the second part of a life span of more than 70 years, although both inhabit roughly the same environment. The fact that cell damage has remarkably little effect during the first part of life, however short or long this may be, may indicate that at this time the damage is efficiently eliminated, for example, by the mending of broken DNA templates, the shedding of cells from epithelia and the destruction of abnormal cells by the immune response they evoke. The pathological changes of middle and old age may then represent more a deterioration in the efficiency of the repair mechanisms than a time-dependent accumulation of cell damage.

In other words these abnormal changes are more likely to be the result of senescence than its cause, and in support of this it has been repeatedly shown that the prevention of senescence by stress is accompanied by the inhibition of carcinogenesis.

My theory can be summarized as follows. In the mammals there is a mechanism which determines the time of onset of ageing and the rate at which it proceeds; this mechanism is probably based in the cells of a single tissue which acts as a pacemaker; this pacemaker is most likely to be a non-mitotic tissue and there is reason to believe that a progressive loss of neurones could of itself lead to the progressive deterioration of the whole body; cell loss is seen in all tissues and in a typical mitotic tissue it is controlled, as also is mitosis, by the homeostatic chalone mechanism; the stronger the chalone action the lower the rate of cell loss and in most tissues so far studied the chalone mechanism is strengthened whenever the concentration of the stress hormones is increased; such an increase in stress increases the life expectancy of laboratory rodents, preserves their nervous and muscular efficiency, and prevents the onset of pathological changes.

One final point may be made. If it is felt that, in order to prolong life, the imposition of stress is unacceptable, the reply may be left to Levi[29] who has shown that "pleasant stimuli evoking amusement are nearly as potent as unpleasant ones" in activating the human adrenals.

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Search for a Human Breast Cancer Virus

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Some human milk contains particles physically identical to the mouse mammary tumour virus. Tumorigenesis in the mouse could serve as a model in the study of human breast cancer.

CARCINOMA of the mammary gland in mouse and man was considered at one time to be primarily a hereditary disease, especially in man, because of its higher incidence in particular family groups. Bittner's discovery[1] of an extrachromosomal factor in the milk of mice indicated that murine mammary cancer was not controlled by genes alone. Mammary tumorigenesis in the mouse was also shown to be affected by hormonal stimulation and to be modified by immune response, and the viral aetiology of this disease in mice is now firmly established. But little is known about the factors involved in the development of carcinoma of the human breast; some widely held ideas, such as the protection conferred on the mother by nursing, have recently been shattered[2-4]. It seems that, as in the mouse, a viral factor is involved in the aetiology of human breast cancer. Results of recent studies on human milk, some of which have been published[5], strongly support this idea.

Human Milk

We fractionated and examined by electron microscopy milk from 212 women. The specimens can be divided into three distinct classes: 156 were from women in the Philadelphia area with no history of breast cancer in their families; ten were from women with a history of breast cancer in their immediate families; forty-six were from the Parsi community of Bombay, included because these women are three times more likely to have mammary tumour than the rest of the population of Bombay[6-8]—it accounts for 49% of all cancer[8] although the overall incidence seems to be no greater than that in other communities[9]. Their ancestors (Zoroastrians) came to India from Persia in the seventh century AD, and because of their strict religious rules they have married exclusively within their own small community.

By a purification procedure already described[5] particles with the same morphological characteristics (Fig. 1) as those that cause breast cancer in mice (B particles) were found in the milk of all three groups, but the incidences in the groups were vastly different. B particles were found in the milk of seven (5%) of the American women with no history of the disease in their families; they were found in the milk of six (60%) of the Americans with a history of the disease in their families; eighteen (39%) of the Parsi women were found to contain the particles in their milk. Some details of the second group are given in Table 1. Two donors of the first group (with no family history of breast cancer) have recently provided second samples of milk after the birth of another child and B particles were again found in both. Structures different from the B particles, possibly representing various types of mycoplasma and other virions[10-12], were also seen in many of the isolates.

Table 1 Donors from Families with Breast Cancer History

Donor No.	Age of donor	Member of family who has had breast cancer	B particles found
1	19	Mother	−
2	24	Mother and grandmother	+
3	18	Mother	+
4	21	Mother and grandmother	−
5	26	Grandmother	+
6	30	Mother and sister	+
7	39	2 maternal aunts	−
8	27	1 maternal aunt	−
9	27	Mother	+
10	26	Mother	+

Failure to find B particles is not conclusive because of the poor sampling provided by electron microscopy.

When this investigation was started, some of the samples of human milk were frozen, but it was found that freezing greatly reduced the bioactivity of mouse milk and damaged the structure of the particles[13]. A procedure was therefore developed whereby human milk could be stored and transported at room temperature. The procedure consisted of adding to the fresh milk an equal volume of a solution containing 400 U of penicillin G, 2,000 μg of neomycin, 100 μg of acromycin, and 200 U/ml. of polymyxin B. Mouse milk prepared in this way could be kept for 5 days at 37° C and for months in the refrigerator without noticeable change in the virions. There was also little change in bioactivity in mouse milk after storage at 37° C for 8 days (Table 2). Bentamycin (Schering, 0.01 ml./ml. of milk) is also a satisfactory preservative.

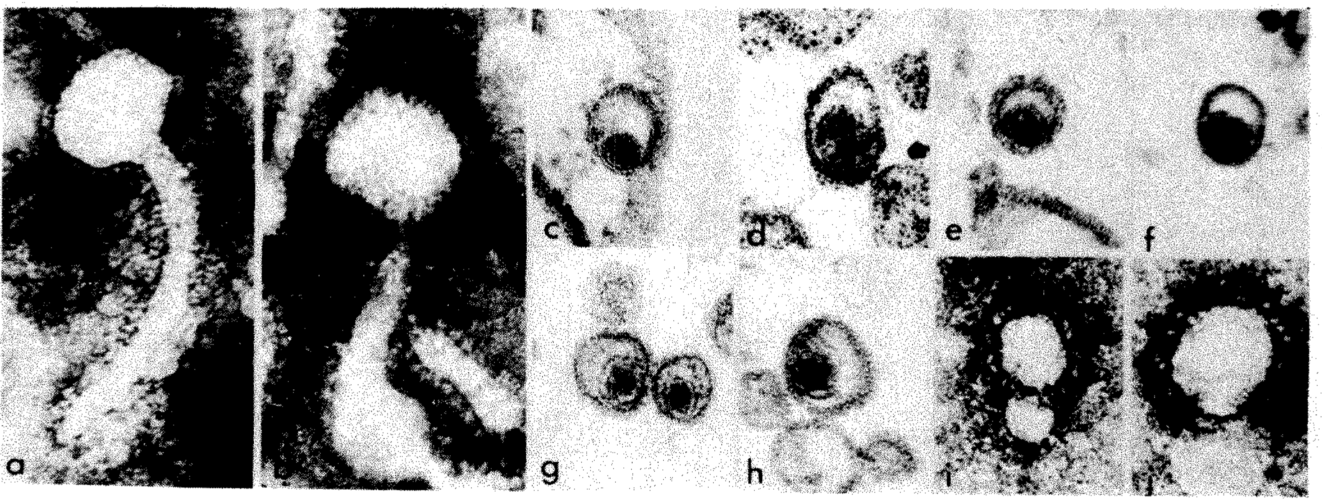

Fig. 1 Particles found in human and mouse milk and in culture fluid. *a*, Negatively stained particle from American human milk; note the long curved tail and knobbed surface protrusions. *b*, Negatively stained particle from RIII mouse milk (× 180,000). *c*, *d*, *e* and *f*, Thin sections of particles from Parsi milks (× 90,000). *g* and *h*, Thin sections of particles from RIII mouse milks (× 90,000). *i* and *j*, Negatively stained particles from fluid of human breast cancer cell culture, but found also in foetal calf serum (× 200,000).

The structure of the intact MTV virion is distinct from all other known structures[5,14]. In negative contrast, the well preserved virion forms a head about 100 mμ in diameter and a tail of variable length. The surface projections on the membrane are different to those of myxo and paramyxoviruses. They are also different from the projections on mitochondrial membranes and from those of any other cellular membrane[14]. They are a little less than 100 Å long and they consist of a stalk 10 to 20 Å in diameter with a 50 Å knob at the distal end. These projections are spaced over the surface of the particle at a centre to centre distance of 70–75 Å.

B Particle and Tissue Culture

Usually virions replicate in the mammary gland[15] or mammary tumours, but proliferation has also been seen in male genitalia[16], thymus[17], thymic[18] and lung[19] tumours and in transplanted mouse ependymoblastoma[20]. Virions and bioactivity can be detected in blood[21,22] and bioactivity can be detected in all tissues of high-tumour-strain mice. Mammary tumour virus (MTV) antigens, but not whole virions, have been reported in spleen cells[23] and Leydig-cell tumours (unpublished results of R. C. Nowinski, N. H. S., L. J. Old, D. H. M. and J. Hilgers), but there is no evidence for a causal relationship between MTV and any neoplasm except that of the mammary gland.

Explants of mouse mammary tumours have been grown in culture for many years[24,25] and a few cell lines have been established[26]. The cells proliferate virus to varying degrees[27]. It has not yet been possible, however, to infect any virus-free cultures with the mouse virus and obtain virion proliferation[28]. Until recently most specimens of human breast cancer obtained from surgery have not survived explantation and few cell lines have been established[29]. The availability of collagenase and new standardized culture media have eliminated most culture problems and permit routine explantation of human breast tumours. Collagenase treatment liberates cancer cells from collagen fibres and prevents overgrowth by connective tissue cells[30].

Table 2 Assays of Incubated Mouse Milk

Treatment	No. positive/No. at risk (%) Dilution 10^{-3}	 10^{-4}
Fresh	2/8 (25)	4/6 (75)
24 h at 37° C	10/10 (100)	10/12 (83)
48 h at 37° C	6/7 (86)	5/10 (50)
96 h at 37° C	8/8 (100)	3/9 (33)
192 h at 37° C	4/12 (25)	6/11 (55)

Skim milk from strain RIII mice was assayed for infectivity in C57CL/Haag mice by the detection of viral antigen in their milk at the third lactation[48]. Before incubation, antibiotics were added to the RIII milk (see text).

Particles covered with knobbed protrusions have been found in culture fluids of primary breast carcinomas[1]. Although these structures have envelopes somewhat similar to those only associated with mouse B particles, they have neither the characteristic size nor shape (Fig. 1, *i* and *j*) and are therefore not considered to be B particles. Identical structures have been observed consistently in concentrates of pooled commercial bovine sera used in the cultures.

Complexity of the Mouse Model

From the beginning of the twentieth century until the early 1930s, while isogenic strains of mice were being developed, it was generally concluded that the occurrence of mammary carcinoma was determined principally by genetic constitution, but in 1933, that reciprocally cross-bred mice of high and low strains were observed to have a cancer incidence that did not follow the laws of Mendelian genetics, but depended primarily on the mother[32,33]. Thirty-five years have passed since Bittner's discovery of the milk factor and, in spite of hundreds of attempts to identify and isolate this factor[34–37], general agreement has been reached on its identification[38–45] only recently. The reasons for the long period of frustration are varied, but the difficulties were finally overcome by recognizing that low-tumour-incidence mice were carriers of MTV which could be potentiated by hormones or other means and that the male sometimes transmitted the virus. More rapid assay procedures[46–49] and improved methods of isolation were developed, and finally, by titrations of isolates, a correlation was found between infectivity and a specific particle[13] (Table 3).

Table 3 Correlations of B Particle Count with Infectivity

Gradient band	ID_{50}/ 0.1 ml.	Antilog ID_{50}/ 0.1 ml.	B particles/ 100 EM quadrants	B particles/ antilog ID_{50}
(1)	$10^{-0.57}$	7.6	50	6·6
(2)	$10^{-1.35}$	54	2,800	51
(3)	$10^{-2.25}$	400	10,000	25
(4)	$10^{-0.75}$	8.8	620	70
(5)	$10^{-0.56}$	7.5	450	60

Resuspended ultracentrifuged pellet from RIII milk was centrifuged on a preformed linear Ficoll density gradient. The contents of the tube were divided into five fractions or bands from top to bottom (column 1). The infectivity of each fraction (column 2) was correlated with B particle counts (column 4) and in the last column the ratio of particles to infectivity was shown to be constant within the errors of the procedure. In band 1, the B particles were difficult to count because of fat globules.

Knowledge of the mouse mammary tumour virus and its role in tumorigenesis can be summarized as follows. (1) Mammary adenocarcinoma has been extensively studied in about a dozen inbred mouse strains. Low tumour strains with a tumour incidence of 0–5% in females and high tumour strains with an incidence of 95–100% as well as strains with intermediate incidences have been developed. (2) Reciprocal crosses between low and high tumour strains produce offspring with an incidence similar to that of the mother[32,33]. There are exceptions, however, and it is concluded that some fathers can transmit the virus and indeed virus particles can be found in male genitalia[16]. (3) Usually the tumour incidence and tumour characteristics can be greatly influenced by foster-nursing newborn litters; that is, the fostered litters tend to have the tumour incidence and tumour characteristics of their foster mothers[1,50]. Again there are exceptions: the litters of two strains GR and C3H-A^{vy}fB retain the high incidence (95–100%) in spite of being fostered on tumour-free strains[51,52]. This has been attributed, with good evidence, to the integration of the viral genome into the sex cells of the parents[53]. (4) Mouse mammary carcinoma is usually transmitted from mother to daughter in the mother's milk. Milk of high cancer strains contains from 10^9 to 10^{12} virus particles per ml. and infectivity remains at 10^{-5} to 10^{-8} dilution. Evidence for natural horizontal transmission is lacking; it is not a contagious disease. (5) Tumorigenic activity may be related to a particular virus particle readily recognizable under the electron microscope. The existence of a sub-viral active entity or a provirus is not yet fully established, and the question of an inhibitor is not settled[37]. (6) The virus seems to be an essential factor in tumour development, but not all mice carrying the virus develop tumours; other factors[54] greatly influence tumour development. Mice carry the virus from infancy when they obtain it in their mother's milk, but they do not usually develop the disease until middle age or later and in some virus-infected strains many never do[55]. (7) It has been possible neither to transfer the virus to any other species nor to infect any normal cells in culture.

Mouse Model applied to Humans

The extensive mouse studies have been made, of course, for the purpose of gaining knowledge of the human disease. There are striking similarities between the disease in the two species. In both there are family groups: in the case of mice this was first recorded by Murray[56] at the beginning of this century. At that time there were no inbred mouse strains, but by selective breeding experiments begun in 1906, Murray obtained an incidence of 18.1% among progeny of cancerous ancestry compared with 8.3% among offspring of non-cancerous ancestry. Ninety-nine female wild house mice bred in the laboratory by Andervont[57] for 10 yr had a mammary tumour incidence of about 6%, little different from that in American women. Although insufficient milk from wild mice has been obtained to confirm the presence of virus particles, it has been shown to contain a milk factor: when a low tumour strain of laboratory mice (BALB/c) was fostered by them, the BALB/c mice became infected and took on the characteristics of a high tumour strain; these fostered mice remain one of the best producers of MTV[58].

Penrose *et al.*[59] studied the incidence of breast cancer in human families and found that there was a significantly greater incidence among mothers and sisters of 510 breast cancer probands but no increased frequency in either sex from other types of malignancy. Similar results were obtained by Smithers *et al.*[60]. In an investigation of 544 women suffering from breast cancer, Anderson *et al.*[61] concluded that sisters of breast cancer patients develop the disease at a rate 1.8 times higher than the controls. Of 1,802 patients of Haagensen[62], 25.8% had female relatives with a history of breast cancer; 9% of the patients' mothers had the disease.

Serious cases of cancer families have been reported for more than 100 y. In 1866 Paul Broca, a French surgeon, reported that ten of the twenty-four women of his immediate ancestors died of breast cancer. Families in which carcinoma of the breast has occurred in three successive generations have frequently been reported. Papadrianos *et al.*[62] state: "The simplest of the many different aspects of familial inheritance is the frequency of the disease in mothers, daughters and sisters of women who develop it". Although some data do not confirm the familial nature of human breast cancer, Clemmesen[63], the leading authority on the statistics of cancer, concludes: "It is difficult to avoid the impression that the scale of such studies . . . has not reached a size matching their task. . . . Nevertheless, as a general conclusion it would seem that heredity of breast cancer has in man been found too often to be explained as due to coincidental occurrence, and is probably as real as in the mouse".

Table 4 Breast Cancer Incidence Rates

Location	Incidence rate
Bombay (Parsi)	51.5
Boston, US	55.0
Glamorgan County, Wales	38.8
Athens, Greece	28.9
Slovenia, Yugoslavia	24.4
Taipei, Taiwan	9.1

Cases per year per 100,000 female population[3]. Japan has approximately the same incidence rate as Taiwan.

It must be pointed out that hereditary and viral transmission is not distinct even in the mouse and much less so in humans; however, most cases of mammary tumour inheritance in mice have been traced to the virus or viral genome.

Mice develop multiple primary tumours, a characteristic which is not thought to be shared by humans, but Haagensen states (personal communication) that of 626 of his patients, studied for a minimum of 10 yr, thirty-six developed a new primary carcinoma of the other breast. The number of cancers of the other breast that would have been expected on the basis of age specific rates for cancer of one breast is 4.9.

The development of mammary carcinoma in both mice and women is influenced by hormones but the influence is complicated. When Lacassagne[64] induced mammary tumours in male mice by the administration of oestrogen in 1932, it was thought that oestrogen might be carcinogenic, but experimentation of the intervening years has led to the conclusion that hormones are only promoting factors and that an initiating agent such as the mammary tumour virus is always necessary[65]. Specialists in cancer of the human breast have come to the same conclusion; hormones alone cannot initiate cancer.

Effect of Nursing

It has long been held that lactation had a significant prophylactic effect on breast cancer, because in countries in which it is rare, nursing is customary and frequently prolonged. Furthermore, there has been an increase in breast cancer in recent years associated with a decrease in breast feeding. A number of studies[2-4] indicate that there is no relationship between the incidence of breast cancer and lactation. The great variation in breast cancer incidence in the different areas of the world, shown in Table 4, is still unexplained. It is possible that, as in the mouse, a mammary tumour virus has something to do with it, and that low, intermediate and high cancer populations have developed naturally.

Implications of Mouse Model

We conclude that the similarities between adenocarcinoma of the breast in mice and women are too extensive to be coincidental and that human breast cancer may also be a viral disease. Moreover, recent studies suggest that human virus may be similar to if not morphologically identical with the mouse virus; sera from breast cancer patients have a neutralizing effect on the mouse virus whereas control sera do not[66]. The mouse model suggests several modes of attack on human breast cancer, although controlled infection studies in which animals are inoculated with infective material, the most productive approach in the mouse, are of course impossible to pursue in man. Retrospective and prospective statistical studies of breast cancer incidence in women, lengthy and unsatisfactory as they may be, can provide data consistent with the notion of vertical transmission of a tumour virus. Other approaches found useful with mice are more promising. Examination of particles similar to or structurally identical with mouse virus by electron microscopy and immunological studies are providing evidence of the existence of such entities in human material. The existence in milk and tumour extracts of antigens related to mammary tumour virus has been demonstrated by means of gel immunodiffusion[67] and by agglutination inhibition of tanned red cells coated with purified virus antigen[68]. Polymerases peculiar to the tumour viruses[69-71] have been found by Spiegelman and Schlom in the mouse virus. Similar demonstrations may be possible with the human virus. Apart from these efforts to demonstrate a virus as the aetiological agent in the human disease, an attack on the tumorigenic process in mice by immune therapy prophylaxis or chemotherapy (including the use of interferon[72] or interferon inducers) seems important since a successful method might be developed for the mouse that could be tested, with minimal risk, in women.

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Colour and Brightness Preferences in Monkeys

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A method has been developed for testing the preferences of monkeys for simple visual stimuli. Preliminary results for colour and brightness have already been obtained.

THE basis of people's everyday decisions is usually "aesthetic" preference. Clothes are chosen for their colour; a bar of soap is chosen for its smell; the route of a journey is chosen for the scenery along the road. Very little is known, however, about these preferences—the stimuli that are preferred cannot be specified in any detail; it is not known how far they depend on genetic, developmental and cultural factors; almost nothing is known about their evolutionary history and little about what biological advantage they bring.

With these general questions in mind, I have investigated the preferences of male rhesus monkeys (*Macaca mulatta*). It is of theoretical importance to know whether any comparable phenomena occur with lower primates. If they do, there will be the practical advantage of being able to study some of the central questions I have listed in an experimental animal, which can be subjected to environmental and physiological control. I have begun by looking at preferences for simple visual stimuli, and wish to describe a method and some preliminary findings.

In studies of "sensory reinforcement" such as those of Butler[1], sensory stimuli have been made the primary goal of the animal's behaviour. I have chosen, instead, to study what happens when the stimuli are made incidental to behaviour which already has an independent goal. I have given a monkey a free choice of alternative behavioural routes to obtain food, each of which is equally efficient but involves exposure to different visual stimuli: to the extent that the monkey chooses one route rather than another, he shows a preference for the associated stimuli.

A monkey was put in a testing chamber where visual stimuli could be back-projected on one of the walls. The chamber contained a single response key and the monkey was rewarded with food for holding down this key for a cumulative period of 100 s, independently of his detailed pattern. The key controlled the presentation of the visual stimuli and the programme ran as follows. In any particular session there would be two alternative stimuli, say *X* and *Y*, which would be produced alternately by successive holds on the key. When the monkey pressed the key first he might get *X*, which would stay on as long as the hold was maintained; when he released the key and pressed again he would then get *Y*, which, likewise, would stay on as long as the hold was maintained; the next press would produce *X*, the next *Y*, and so on. To exercise a preference the monkey had simply to hold the key down when he preferred the current stimulus and release and press again when he did not.

The testing chamber (Fig. 1) was a small rectangular box, 80 × 65 × 45 cm, painted black inside. At one end of the chamber, covering the wall, was a ground glass screen, 45 × 45 cm, on which the alternative stimuli were projected from either of two projectors. The stimuli could be varied by changing the slides in the projectors. Bars across the chamber confined the monkey to a relatively small compartment at the opposite end to the screen so that he sat facing the screen at a convenient visual distance from it, about 40 cm. In front of him was a sloping dashboard bearing the response key and

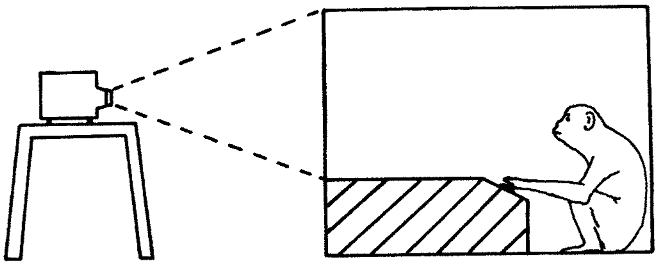

Fig. 1 Testing chamber.

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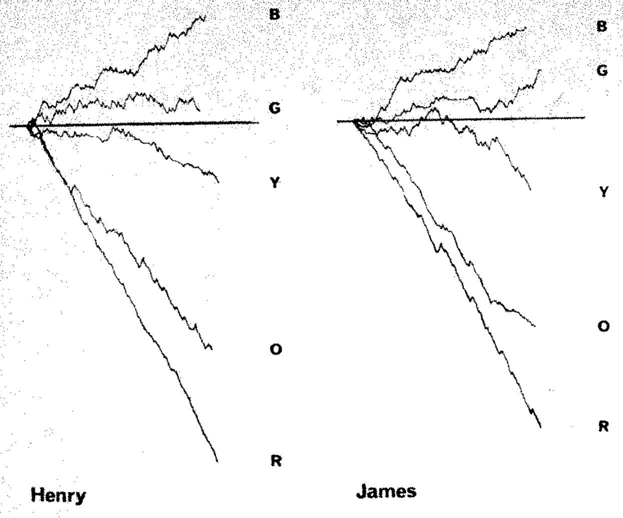

Fig. 2 Sample records from tests for colour preference. The test stimuli were homogeneous coloured fields of equal subjective brightness, paired in each case with a standard white field of the same subjective brightness. The lines show how the monkey divided his time between the test and the standard stimuli: the recording pen moved upwards at 75° when the test stimulus was on and downwards at 75° when the standard comparison stimulus was on, so that upward slopes represent positive preference and downward slopes negative preference relative to the standard. B, blue; G, green; Y, yellow; O, orange; R, red.

below that was a pellet tray. In the roof was a small pea-bulb which served as a dim houselight during time-out periods. When the monkey first entered the chamber the houselight was on and the response key was inoperative. After a short while the houselight went out and the response key became effective. The monkey was then free to press the key as he chose, alternating between the two stimuli and holding either as long as he wished, although with the constraint that neither was to stay on longer than 10 s or else it was automatically terminated and he had to release and press again (in practice this limit was very rarely reached). When he had clocked up 100 s of total response, the houselight came on again and the key was inoperative for the next 50 s during which time five banana pellets were delivered to the tray. The houselight then went out, the key became effective and the programme was recycled. At the end of ten such cycles (1,000 s of total response), the houselight came on finally and the sequence was terminated. In the course of the experiment measurements were made of the total number of alternations between the two stimuli and the total time spent in the presence of each. The monkey's performance was also displayed on a pen recorder which showed from moment to moment how he divided his time between the two stimuli: the recording pen moved upwards at an angle of 75 degrees when one stimulus was on and downwards at an angle of 75 degrees when the other was on, so that the overall slope indicated the preference.

The principal results obtained so far concern colour and brightness preferences. The stimuli here were homogeneous fields of light filling the whole screen, with brightness and colour determined by filters in the projectors. For the brightness study the fields were white and ranged in brightness in eleven steps from 0.1 to 1.7 log foot-lamberts. For the colour study the fields were coloured red, orange, yellow, green and blue (Kodak Wratten filter numbers 25, 22, 12, 58 and 38A, respectively) and were adjusted in subjective brightness with an SEI photometer to 0.9 log foot-lamberts for the human eye, which has a sensitivity curve almost identical to that of the rhesus monkey[2]. So that all measurements of preference should be directly comparable, a white field of 0.9 log foot-lamberts was used as a standard stimulus with which to pair each other stimulus to measure the relative preference.

Four monkeys, all adolescent males imported from India about one year previously, took part in this experiment. Outside the testing sessions they were housed in pairs in cages in the home colony and were fed on a diet of chow which was freely available. One pair, Henry and James, had more extensive testing than the others, and the results for these two will be given in detail. They were tested 6 days a week, twice a day, for colour preference in the morning and for brightness preference in the afternoon. The different levels of brightness and the different colours were tested in a random order which was the same for both monkeys. The set of brightness stimuli was run through twice consecutively and the set of colour stimuli three times, that is, for each level of brightness two measurements were made separated by about 2 weeks, and for each colour three measurements separated by about 1 week.

About 15 days' training with irrelevant stimuli was given to familiarize the monkeys with the contingencies of the testing situation. With this preliminary experience the pattern of performance settled down and became very constant. The monkeys responded usually without interruption and completed the 1,000 s of stimulus presentation in about 1,300 s (not counting time-out periods). During this time they alternated rapidly between the two stimuli, on average about 400 times. The number of alternations was higher overall for the brightness tests than for the colour tests (means of 439 and 354, respectively: $P<0.01$ on a t test), but otherwise it had little relationship either to the nature of the stimuli or, surprisingly, to the degree of preference shown: an increase in preference could mean either an increase in the time for which the preferred stimulus was held on or a decrease in the time for which the non-preferred stimulus was held on, and the sum of these periods—the time for two alternations—need not, and did not, vary systematically. The preferences tended to be quite stable from the beginning to the end of a session; there were no marked swings, and the monkeys showed little sign of losing interest in the stimuli even when the sessions were extended to twice their usual length. Rapid alternation in combination with a basically stable preference led to almost linear performance records.

Figs. 2 and 3 show for Henry and James some sample records from individual sessions, and Fig. 4 shows the mean

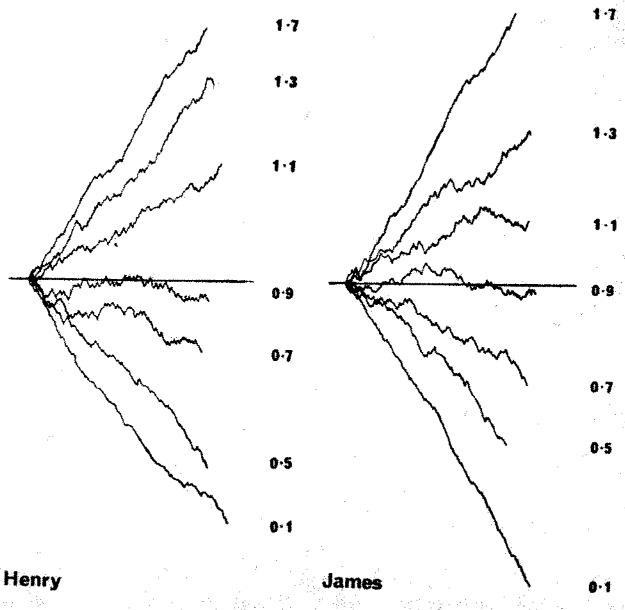

Fig. 3 Sample records from tests for brightness preference. The test stimuli were homogeneous white fields of different brightness. The numbers give the brightness of the test stimuli in log foot-lamberts.

preferences for each test stimulus in terms of the amount of time per 1,000 s session spent with that stimulus as opposed to the standard stimulus. Table 1 gives the results of three-way analyses of variance on the preference and alternation scores.

Table 1 Results of Three Way Analyses of Variance

Source of variation	Degrees of freedom	Variance ratio
A Preference scores		
(i)		
Brightness levels	10, 10	509*
Repeated measurements	1, 10	3.13
Monkeys	1, 10	0.00
(ii)		
Colours	4, 8	112*
Repeated measurements	2, 8	0.45
Monkeys	1, 8	0.02
B Alternations		
(i)		
Brightness levels	10, 10	0.77
Repeated measurements	1, 10	1.05
Monkeys	1, 10	1.03
(ii)		
Colours	4, 8	0.51
Repeated measurements	2, 8	0.87
Monkeys	1, 8	2.79

* Significant at 0.1% level; no other results were significant at 5% level.

Both monkeys had strong preferences related to both brightness and colour. These preferences were not, as might have been expected in a two-choice situation, all or none, but were finely graded. The brightness preferences were monotonically related to brightness over the range used, and, more surprisingly, the colour preferences were monotonically related to wavelength. Repeated measurements were highly consistent, and there was remarkably little variation even between the two monkeys.

The other pair of monkeys, who were actually rather younger than Henry and James, showed similar strong and reliable preferences. Their preferences were quantitatively close to those of Henry and James in the case of brightness, but were smaller in the case of colour, although the same rank order of colours obtained.

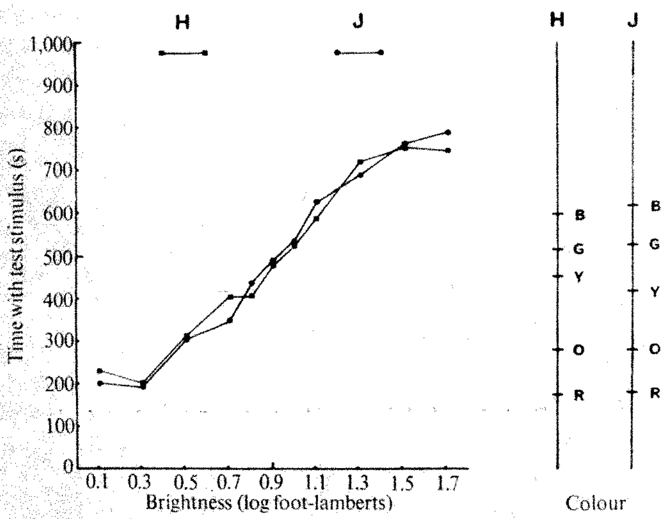

Fig. 4 Mean preferences on the brightness and colour tests, averaged over two sessions for brightness and three sessions for colour. The ordinate gives the amount of time per 1,000 s session spent with the test stimulus as opposed to the standard stimulus.

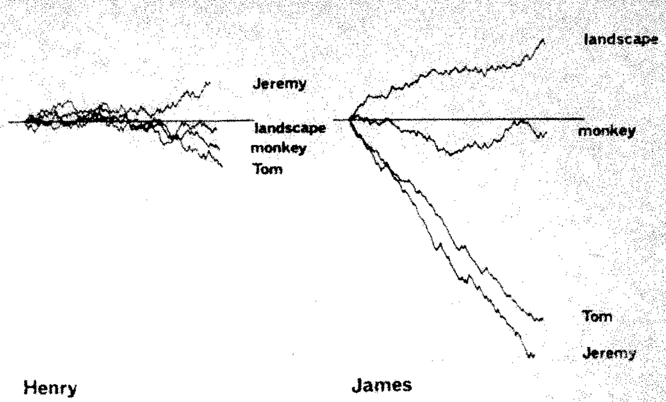

Fig. 5 Sample records from tests for picture preference. The test stimuli were coloured photographs of equal subjective brightness to the standard stimulus. Jeremy, the laboratory photographer; Tom, the animal cleaner; monkey, a frightened monkey in a cage; landscape, a mountain in Connemara.

To follow up the striking similarity in the behaviour of the different monkeys, I made additional tests with other kinds of stimuli. It was found, predictably, that with more complex and meaningful stimuli this similarity no longer held. Fig. 5 shows sample records from sessions where the stimuli were "pictures" instead of homogeneous fields. The pictures were coloured photographs of people, animals and outdoor scenes, adjusted in overall brightness (when defocused) to 0.9 log foot-lamberts; as before, each was compared with the standard white field. With these stimuli the preferences of individual monkeys diverged. Henry, for example, was relatively indifferent to a picture of Tom, the cleaner, whereas James apparently disliked it; of the other monkeys, one strongly liked the same picture, whereas the other disliked it as much as James.

These results as a whole show the method to be an effective way of demonstrating and measuring visual preferences. The specific findings raise many points for further exploration. (1) To what extent, if at all, are the demonstrated preferences peculiar to this testing method? In particular, what is the significance of using primary reinforcement to maintain the key pressing behaviour? Would the results have been the same had some other reward than food been used or had it been practicable to use no reward at all? (2) What are the formal characteristics of the preferences? For example, if stimulus *A* is preferred to *B*, and *B* is preferred to *C*, does it follow that *A* is preferred to *C*? Or, if stimulus *D* is strongly preferred to *E* and only weakly preferred to *F*, does it follow that *F* is preferred to *E*? (3) What is the origin of the preferences? Can the similarity in the brightness and colour preferences of different monkeys be taken to mean that these preferences are species-specific and independent of individual experience, or could it be that these monkeys happened to have had the same experience at some critical period in their early life? (4) How far are the preferences a function of a particular set of environmental and bodily conditions? How would they be affected, for example, by changes in ambient temperature, changes in time of day, or changes in motivational state? (5) What is the adaptive value of the preferences? In so far as they are innate, what significance do they have for a monkey in the wild?

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LETTERS TO NATURE

PHYSICAL SCIENCES

Terrestrial Spectroscopy by a Cryogenic Gravity Meter

LATE in the nineteenth century and early in the twentieth century, British scientists such as Lamb[1] and Love[2] had made theoretical predictions about the free oscillations of the Earth. The gravest mode was calculated to be about 1 h. Benioff[3] in 1954 surmised that a signal with a 57 min period recorded during the Kamchatka earthquake might be the grave mode of the free oscillations of the Earth. Pekeris[4] and his colleagues, stimulated by such predictions, were able to calculate the period of free oscillations of the Earth for a large number of modes, and these theoretical predictions were confirmed for the first time[5,7] after the great Chilean earthquake of May 22, 1960. Easier numerical integration techniques for calculating different models of the Earth have since been introduced[8] and other earthquakes—among them, the Kurile Islands earthquake[9] of October 13, 1963, the great Alaskan earthquake[10] of 1964 and the Rat Island (Aleutians) earthquake[11] of February 4, 1965—have confirmed some of the observations made during the Chilean earthquake. Recently, it has been possible[12] to record the spheroidal oscillations of the Earth from earthquakes of magnitude 6.5.

I have been developing a cryogenic gravity meter in the past 5 years[13] with the cooperation of Professor William Fairbank of the Stanford University physics department. With this instrument, we have recorded a large number of spheroidal oscillations of the Earth over three different periods. The signal ranges from 2 dB to 9 dB above the mean of the record. Several of these peaks are over the 95% confidence limit.

The instrument has a 1 inch hollow niobium sphere suspended in a cylindrically symmetric magnetic field with a suitable magnetic gradient. The superconducting hollow sphere behaves as a diamagnetic element. The magnetic field and the field gradient are adjusted so that upward magnetic push on the ball is balanced by the pull of gravity. In this way, the hollow sphere is freely suspended at the centre of the instrument. The initial raising of the ball is monitored by a special photosensitive device which can operate at liquid helium temperature. The magnetic field and the field gradient are produced by superconducting coils which are made persistent after adjusting the datum of the hollow sphere. A mu-metal canister and a niobium cylinder serve to shield the instrument from external magnetic perturbations.

An independent detection module, using a double Josephson's junction (also known as SQUID) (see ref. 14 and also A. Hebard, personal communication), senses the flux change produced by the motion of the hollow sphere. (The hollow sphere in this present arrangement is immersed in liquid helium.) The detection module can sense a motion of less than one Angström (0.1 nm). A feedback circuit provides a sufficient negative signal so that the Josephson's junction effectively remains in the same magnetic environment, which is accomplished with the aid of a phase-sensitive detector. The system has been calibrated and has proved to have a large linear dynamic range. A portion of the signal is fed to a chart recorder, which depicts the true motions of the suspended sphere. The system has a theoretical sensitivity of about 15×10^{-12} cm/s^2. No measurable drift of the detection module has been recorded over the period of 2 h when the instrument is functioning properly (my unpublished observations).

The analog records obtained from a chart recorder are digitized, after which a Fourier transform is performed on the data. A close inspection of the plot of the period and amplitude of the data reveals four independent types of evidence, indicating that the spheroidal oscillations of the Earth have been recorded continuously at Stanislaus State College. These evidences are discussed below.

(1) A large number of the strong peaks coincide with the observed periods reported by other investigators. However, this evidence can be questioned, since some unknown strong peaks also have been observed that may be overtones. As far as I know, they have not yet been reported by other investigators (Figs. 1, 2 and 3).

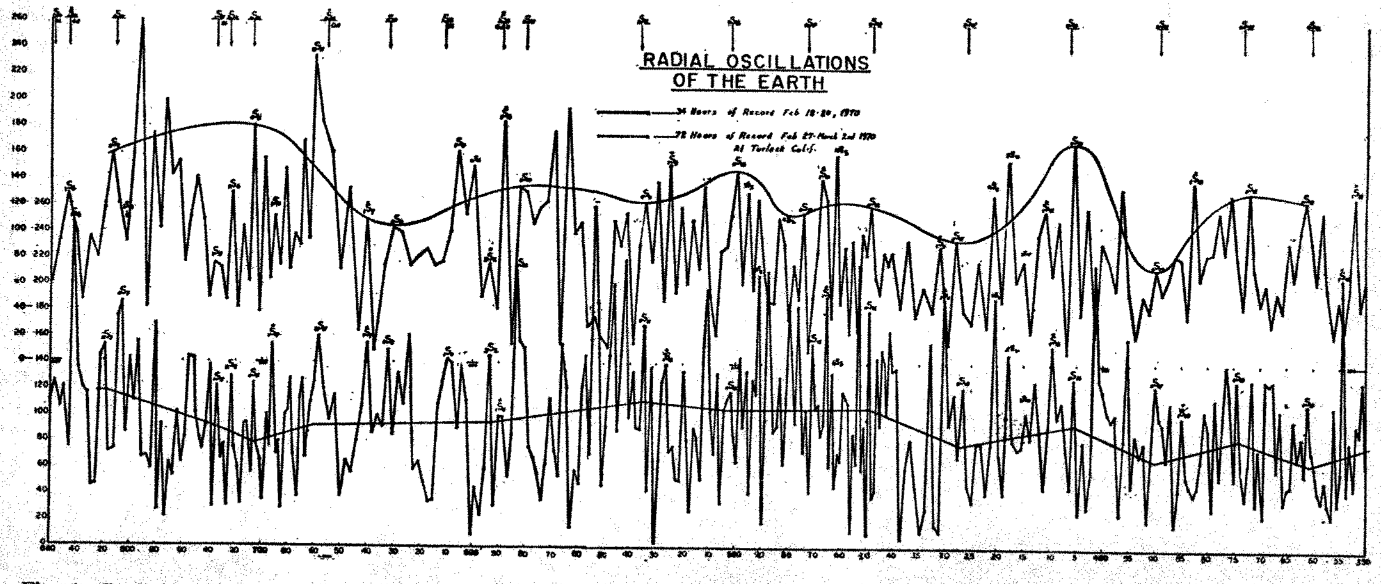


Fig. 1 Radial oscillations of the Earth. Top: 34 h of record February 18–20, 1970. Bottom: 72 h of record February 27–March 2, 1970.

(2) In all three independent records of February 18–20, February 27–March 2, and July 31, 1970, I have observed clearly the splitting of the ${}_0S_2$ mode. (In the three experiments, continuous records were obtained for 32, 72 and 18 h respectively.) Inevitably, the main line is observed as a trough. This splitting, which is due to Earth rotation, should and did yield a trough for the main line of 3,233 seconds because of the geographic location of Stanislaus State College. Similar splitting is observed for the ${}_0S_3$ mode. This independent evidence cannot be taken as a chance, since it has been observed repeatedly over three independent observations (Fig. 4).

(3) A striking feature of the first two recordings which are

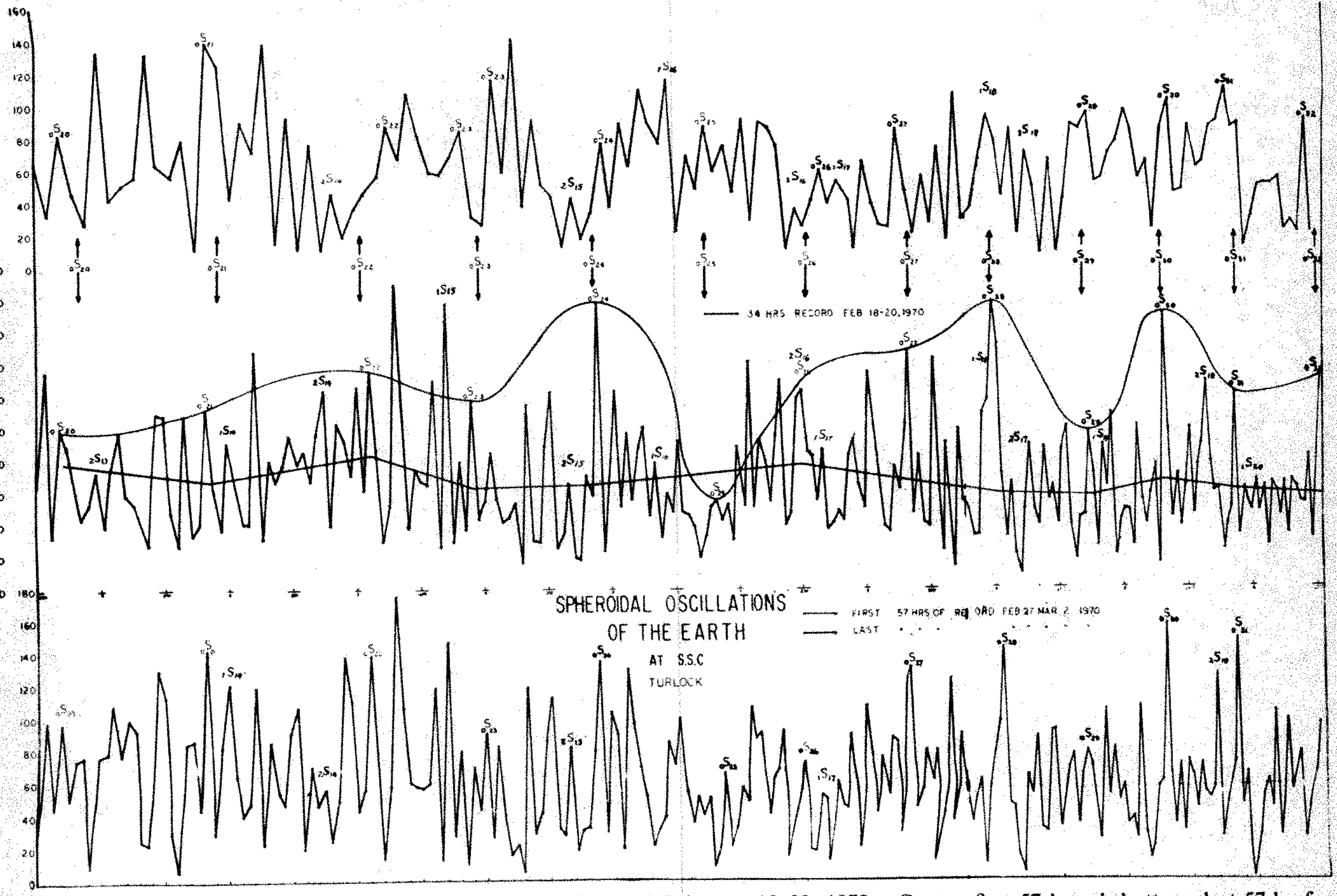
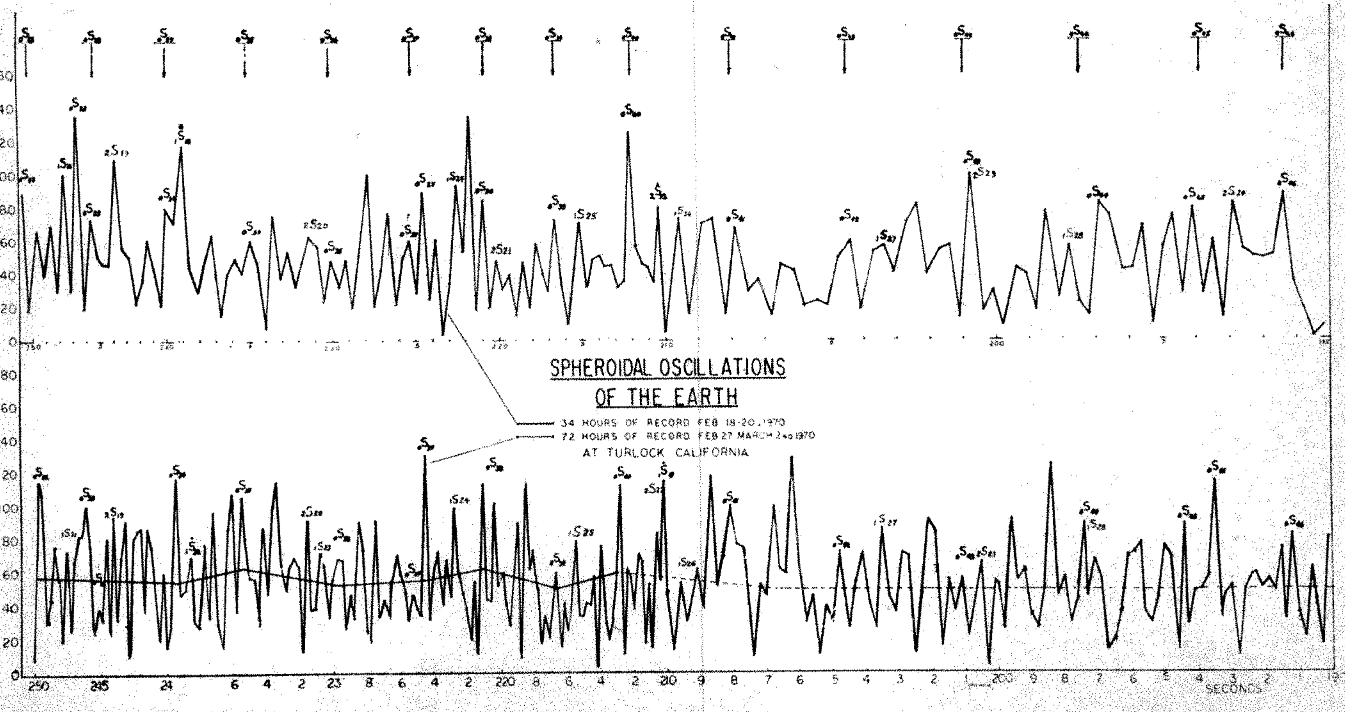


Fig. 2 Spheroidal oscillations of the Earth. Top: 34 h of record February 18–20, 1970. Centre, first 57 h and, bottom, last 57 h of record February 27–March 2, 1970.



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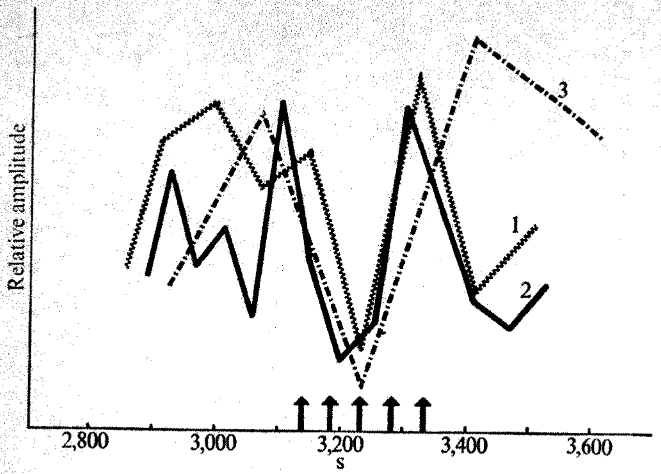

Fig. 4 Degeneration of ${}_0S_2$ due to Earth rotation. Experiment 1, February 18–20, 1970. Experiment 2, February 27–March 2, 1970. Experiment 3, July 31, 1970. Degeneration $2l+1$; $l=2$; number of lines = 5.

reported here are the variations of amplitudes as we move from even harmonics to the odd harmonics. In the first experiment, during February 18–20, 1970, it was observed that the even harmonics from ${}_0S_8$, ${}_0S_{10}$ and all the way to ${}_0S_{18}$ have consistently higher amplitudes when compared with ${}_0S_9$, ${}_0S_{11}$ and ${}_0S_{19}$. In the second experiment, the same phenomenon is observed in the region of ${}_0S_{20}$ to ${}_0S_{32}$, where the even harmonics again have greater amplitudes than the odd harmonics. A similar but more dramatic effect was recorded by R. D. Moore *et al.*[12] and can be seen between ${}_0S_{22}$ to ${}_0S_{38}$ in Figs. 3 and 4 of their article. At present, I know of no theoretical reason why more energy should be preferentially coupled to the even harmonics; however, this is an observed fact that may not occur frequently.

(4) The similarity between our own observations and occasionally with those of others as far as the overtones could be identified is also significant. Some of the overtones seem to be close to the fundamental ${}_0S_n$ harmonics.

After a close analysis of the data, it seems that the instrument can detect spheroidal oscillations of the Earth due to earthquakes of magnitudes 7, 6, and 5.5 and possibly more subtle continuous effects such as energy coupled to these modes by the Moon's tide, and so on. In Table 1, the observed data for all three experiments are compared with the recorded data reported by other observers; our results are well within the spread of the data recorded during the Chilean and the Alaskan earthquakes of 1960 and 1964 respectively[15].

Table 1 Measured ${}_0S_n$ Modes (Periods in Seconds)

n	F. Press[15]	Present observations Series 1	Series 2	Series 3	John Derr[15]
0	1,227.64	1,228.80	1,233.70		
2	3,237.0	3,233.0	3,233.0	3,233.68	3,233.30
3	2,137.2	2,118.6	2,133.33	2,118.60	2,133.56
4	1,549.2	1,536.0	1,551.5	1,536.0	1,547.16
5	1,191.6	1,193.0	1,197.7	1,204.7	1,193.30
6	964.2	975.23	957.0	960.0	963.94
7	811.2	813.77	806.3	808.4	811.67
8	705.6	706.20	706.2	706.2	707.57
9	634.2	630.15	632.09	633.4	634.01
10	577.74	582.37	583.47	579.6	580.04
11	535.02	534.26	534.72	534.2	536.46
12	501.72	499.51	501.96	503.6	502.03
13	472.50	474.44	471.89	472.6	473.05
14	447.90	448.46	449.12	448.46	448.37
15	426.12	428.15	426.66	426.66	426.19
16	406.68	405.54	405.54	406.88	406.54
17	389.52	390.09	390.09	388.86	389.37
18	373.86	372.36	374.40	372.36	373.39
19	358.88	360.35	361.20	359.28	360.57
20	346.68	345.17	349.48	349.09	347.39
21	335.70	336.65	336.84	335.70	335.80
22	324.60	322.52	324.05	323.37	325.07
23	315.36	316.70	315.56	315.08	315.11
24	306.30	305.67	306.12	305.67	306.10
25	297.54	297.53	297.0	too low	297.54
26	289.62	288.45	290.08	289.8	289.48
27	281.64	282.46	281.71	280.5	282.38
28	275.28	275.51	274.90	273.1	274.87
29	268.14	267.71	267.71	267.13	268.27
30	262.08	261.45	261.89	261.44	261.94
31	255.96	257.07	256.32	254.94	256.02
32	250.02	250.78	249.75	249.75	250.09
33	245.10	246.74	246.15	244.78	245.30
34	239.52	240.00	239.53	239.06	239.87
35	235.20	234.95	235.67	234.50	234.51
36	229.74	230.11	229.85	229.2	229.66
37	224.58	224.64	224.56	222.6	224.75
38	220.26	221.00	220.45	220.2	220.08
39	216.72	216.72	216.83	216.33	216.45
40	212.09	212.23	213.00	212.59	212.09
41	208.50	208.62	208.13	208.2	207.88
42	204.30	204.46	204.60	204.8	204.54

Table 2 Measurements of Known Overtones (Periods in Seconds)

Mode	Slichter[6]	Present observations Series 1	Series 2	Series 3
${}_1S_2$	1,479	1,480.48	1,473.4	1,498.53
${}_1S_3$	1,060.8	1,059.3	1,066.67	1,059.31
${}_2S_2$	904.2	902.2	902.3 898.8	903.53
${}_2S_3$		819.2	819.2	819.2 (weak)
${}_1S_4$	858.8	847.44	842.8	841.64
${}_1S_5$	734.4	735.81	734.05	731.43
${}_2S_4$	724.8	722.82	723.67	
${}_2S_5$	660.0	660.64	658.20	667.82 660.64
${}_1S_0$	607.80	605.32	607.72	602.35
${}_3S_2$	580.2	587.94	588.50	590.77
${}_1S_8$	557.3	563.67	564.18	563.67
${}_1S_{10}$	466.6	465.45	465.45	465.45

Table 3 Possible Unknown Overtones (Periods in Seconds)

	Series 1	Series 2	Series 3
1	1,280	1,280	1,304 1,280
2	568.89	570.47	568.88
3	563.67	654.18	563.67
4	546.13	546.13	548.47
5	525.13	525.13	
6	512.00	512.00	512.00
7	495.48	495.88	
8	491.52	491.13	491.52
9	483.78	483.02	480.00
10	467.42	466.5	
11	465.45	465.45	465.45
12	455.11	453.10	455.11
13	420.82	420.53	423.7
14	417.96	417.96	417.96
15	410.97	409.6	
16	408.23	407.97	406.89
17	402.88	401.57	401.57
18	400.26	400.0	
19	396.38	397.67	396.38
20	378.09	378.56	381.60
21	375.78	376.47	374.63
22	362.48	362.48	
23	341.33	340.76	341.33
24	322.50	322.01	323.36
25	312.67	311.72	311.88
26	304.16	304.50	305.67
27	300.44	299.85	301.88
28	294.68	294.25	
29	278.0	278.64	276.78
30	245.76	245.34	
31	243.8	243.20	
32	186.46	186.35	
33	185.34	185.00	185.06

In Table 2 are given the observed known overtones, while in Table 3 a number of lines that have been observed on three experiments are reported. Some of these lines are the dominant peaks on the record. Many of these lines are thought to be overtones not so far observed and which cannot at present be identified for lack of theoretical data based on a model of the Earth.

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Doppler Velocity Measurements using White Light

VELOCITY measurements, based on observations of the Doppler shift in frequency of radiation scattered by moving objects, have been made using various optical arrangements (for example, refs. 1–6). The coherency requirements of the illuminating radiation have been considered by Rudd[5], who concluded that conventional (that is, not laser) light sources could, in principle, be used. Until recently, however, all proposed optical systems have required such critical alignment or small effective source size (to provide sufficient spatial coherence) that the use of conventional light sources was impractical. Consequently, laser light sources have had to be used exclusively. This is now not necessary and it is demonstrated here that the schlieren-interferometer arrangement proposed by Schwar and Weinberg[7,8] can be used even with a white light source. To show that Doppler shifts in frequency that are very much smaller than the line width of the illuminating radiation can be detected, the velocity of a slowly moving pendulum bob was measured.

Fig. 1 shows all the details of the optical system. The detector, D, records the beat frequency, ν_b, produced by the interference of the two differentially Doppler shifted beams selected by the apertures A_1 and A_2 in the schlieren blind, S. If θ is the angle between the two beams scattered by the same point on the moving object, the observed beat frequency is given by

$$\nu_b = \frac{u\theta}{\lambda} \tag{1}$$

where u is the velocity of the scattering point perpendicular to the transluminating beam, and λ is the effective wavelength of the source. It has been shown[8] that this beat frequency can be interpreted as the intensity oscillations that occur when an interference fringe pattern moves across the front of a point detector. The velocity of these fringes is Mu, where M is the magnification of the test space at the detector, and so ν_b is also given by

$$\nu_b = \frac{uM}{\lambda_i^*} \tag{2}$$

where

$$\lambda_i^* = \frac{\lambda}{M\theta} \tag{3}$$

is the fringe spacing at the recording plane. It follows that u can be determined by measuring M, λ_i^* and ν_b.

The positioning of D is achieved by removing S and locating the corresponding image point at which the velocity measurement is required. On replacing S the detector sees a spatially filtered image of the test space. Fig. 2*a* shows such an image of a suspended droplet. Figs. 2*b* and *c* are filtered images of a single straight edge and rod respectively. All were recorded with the optical system at a magnification of 2.64 on Ilford R52 panchromatic plates using a 12 V 50 W tungsten–halogen filament lamp as a light source. Measurements made on the original negatives gave a fringe spacing of 1.050±0.005 mm.

The fringes shown in Fig. 2*b* are similar to Young's white

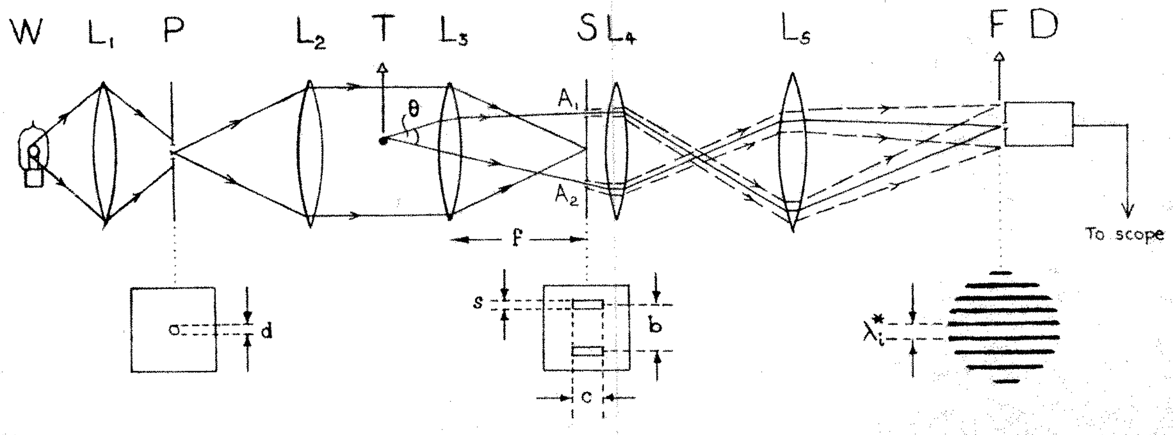

Fig. 1 Schlieren-interferometer optical arrangement. W, 50 W tungsten–halogen lamp; P, screen with pin-hole; T, moving scatterer; S, schlieren blind; A_1, A_2, selective apertures; F, spatially filtered image of moving scatterer, that is, moving fringe pattern; D, photodetector; L_1, condensing lens; L_2, collimating lens; focal length 173 cm; L_3, schlieren lens, focal length 173 cm; L_4, first imaging lens, focal length 50 cm; L_5, second imaging lens, focal length 10.8 cm; d, 1.00±0.05 mm; s, 0.40±0.05 mm; b, 2.50±0.05 mm; c, 2.20±0.05 mm; λ_i^*, fringe spacing.

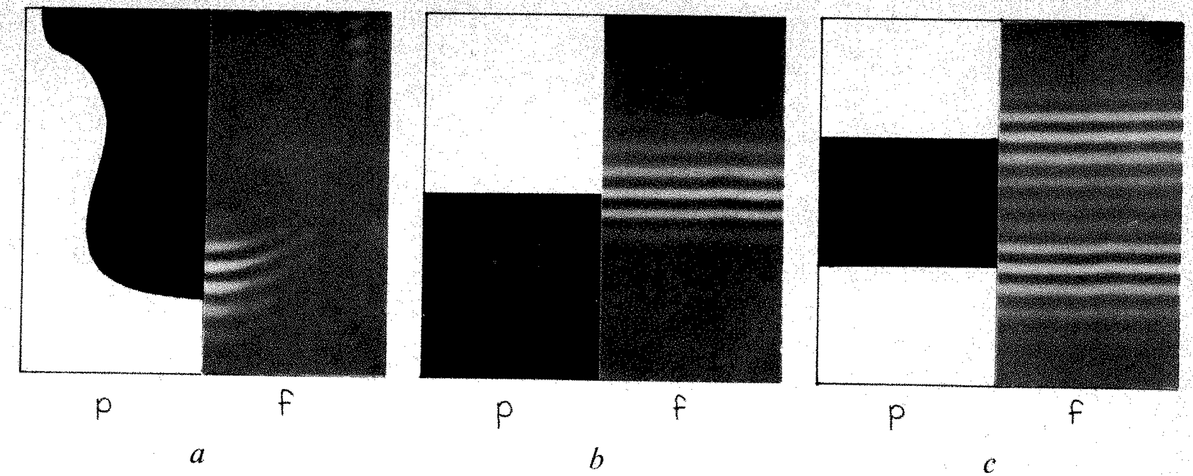

Fig. 2 White light spatially filtered images of various test objects; p, profile of test object; f, filtered image of test object. *a*, Suspended droplet; *b*, single straight edge; *c*, rod.

light interference fringes. The number of fringes, N, arising from a single scattering point is given by

$$N = \frac{2\lambda}{\Delta\lambda} \tag{4}$$

where $\Delta\lambda$ is the effective line width of the source. In the case of an extended scatterer the number of fringes will be greater than this, being determined by the number and separation of the scattering points. Fig. 2*c* shows, in the case of a 2.2 mm diameter rod, that at least eleven white light interference fringes are formed in its filtered image. It follows that more accurate beat frequency (and hence velocity) measurements can be made on moving extended scatterers than on moving point scatterers. Fig. 3 shows an oscilloscope trace of the white light beat frequency signal produced by an extended scatterer (in the form of three 0.2 mm diameter wires irregularly spaced but roughly parallel to each other) 3 mm wide attached to the bottom of a pendulum moving across the transluminating beam. In this case, the number of detectable oscillations is ten. The beat frequency was detected with an EMI 9529A photomultiplier, fitted with a 0.2 mm entrance aperture, and the output voltage developed across a 5 kΩ load resistor was displayed on a 547 Tektronix scope fitted with a 1A7A plug in. The H.T. on the photomultiplier was set to 1.55 kV. As the sweep speed was 0.2 s cm^{-1} the average beat frequency corresponded to 2.85 ± 0.05 Hz, and so the velocity given by equation (2) was 1.13 ± 0.03 cm s^{-1}.

The effective wavelength of the light used in this measurement, calculated from equation (3), with θ put equal to b/f (where b is the separation of the selective apertures A_1 and A_2 and f is the focal length of the schlieren lens), corresponded to ~ 5750 Å. Taking N as ~ 6 for a point scatterer the effective line width of the light source, given by equation (4), was ~ 1900 Å (that is, $\sim 1.7 \times 10^{14}$ Hz).

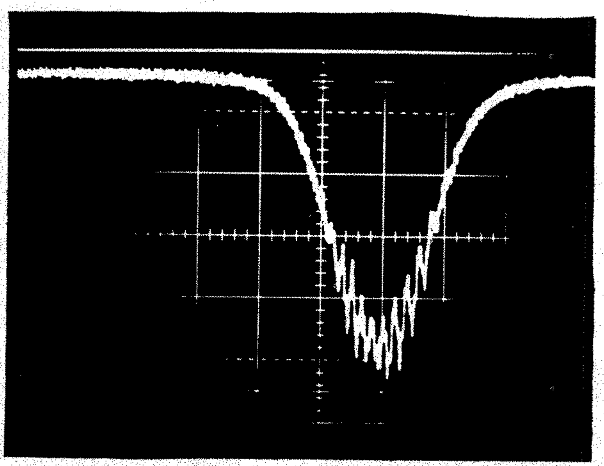

Fig. 3 White light Doppler beat frequency oscillogram trace. Scale 0.2 s cm^{-1} and 10 mV cm^{-1}.

For formation of the maximum possible number of fringes the beam width at the recording plane must be greater than the width of the interference pattern. As the width of the two overlapping beams is determined[9] by the amount of diffraction caused by the selective apertures A_1 and A_2, this will occur only if

$$\frac{b}{s} \geqslant \frac{\lambda}{\Delta\lambda} \tag{5}$$

where s is the width of the selective aperture. But b/s should not be made too large as this will result in an unnecessary reduction in the amount of light falling on the detector. For the system described above $b/s \simeq 5$ and $\lambda/\Delta\lambda \simeq 3$.

The precision of a Doppler velocity measurement depends ultimately on the number of fringes that pass across the point detector. Ideally, N should be made as large as possible. However, if N is increased by decreasing the effective line width of the source the spatial resolution of the measurement decreases. This is because the distance, w_o, over which the velocity measurement is made is given by[9]

$$w_o = \frac{N\lambda}{\theta} \tag{6}$$

and the depth of focus, l, is

$$l = \pm \frac{N\lambda}{\theta^2} \tag{7}$$

Consequently, if high spatial resolution is required θ must also be made as large as possible. As the intensity of the scattered light generally decreases with increasing θ, its upper limit will eventually be set by the brightness of the light source and sensitivity of the detector. Although it has been demonstrated that a small, 50 W, incandescent filament lamp can be used for Doppler velocity measurements there are, of course, very much brighter thermal sources available. It seems, therefore, that even if a laser light source were unavailable, it should be possible, using, for example, a high pressure xenon or mercury vapour discharge lamp, to carry out precise Doppler velocity measurements of high spatial resolution.

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Possible Tertiary Age for Some Antarctic Cirques

SOME large cirques cut into the ridges above the Wright Valley, in the McMurdo Oasis, Antarctica (77° 30′ S, 161° E), are now free of ice and are below the permanent snow line (Figs. 1 and 2). Present day precipitation is approximately 100 mm of snow per year; hence it is a desert region into which the Wright Upper Glacier can only intrude 8 km before ablation losses exceed the supply of ice from the polar plateau. The cirques must have been cut during a local glaciation, not a continental one, because, during a rise of the ice of the polar plateau and a spreading of the ice sheet, precipitation in the area would be reduced even below that of the present, and even at times of lower level of the polar plateau there is little likelihood of significantly higher precipitation than at present. The latter conclusion is supported by evidence from the Taylor Valley, 20 km south of the Wright Valley, where that much of the valley has been ice free for at least 2.7 m.y.[1].

The processes responsible for cirque cutting are not fully understood[2]. There are four principal theories of cirque erosion of which three are concerned with glaciers of warm temperate areas: the bergschrund theory[3] involves diurnal freezing and thawing at the base of the bergschrund; the meltwater theory[4,5] stresses the importance of meltwater and rainwater running down the backwall of the cirque, freezing into rock crevices and shattering the rock; the rotational slip theory[6] involves the sliding of a cirque glacier over its bed and the abrasion by debris included in the sole of the glacier. These theories are all concerned with cirque glaciers which consist of ice the temperatures of which at any depth are at pressure melting-point for that depth, apart from a surface layer of cold ice, up to 20 m or so thick, which is cooled by the atmosphere well below the freezing point in winter. The fourth theory[7] is concerned with the boundary between cold ice (that is, ice with a temperature well below 0° C because of its cold environment) frozen to the bedrock, and wet ice close to the pressure melting point. This boundary would oscillate slowly in response to external conditions and freeze–thaw action at the 0° C boundary would cause shattering of the rock in the cirque walls and floor. This theory, like the preceding three, is essentially concerned with glaciers in which the dominant processes occur at temperatures around 0° C and, according to these theories, glaciers composed of colder ice will not provide favourable environments for erosion processes.

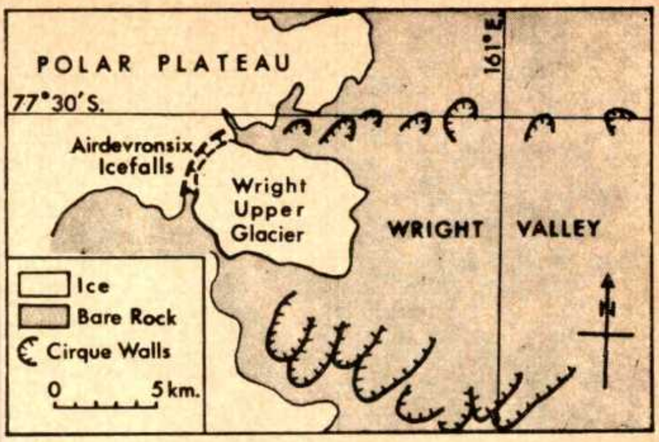

Fig. 2 Location of the ice-free cirques of the upper Wright Valley, Antarctica.

The cirque and small valley glaciers of the McMurdo Oasis are composed of ice with a temperature of about −20° C. Field observations show that at present they are not eroding their beds. Any meltwater draining from them is clear (rock-flour was not observed) and they slide or creep over frozen rock or frozen old moraine which they can neither abrade nor move; hence, contemporary moraines at the sides and snouts of glaciers are composed of debris which has fallen on to the glaciers from cirque or valley walls.

The cirques of the McMurdo Region must have been cut when Antarctica experienced a temperate climate. Assuming that the altitude of the cirque floors (1,600 to 1,800 m) has been constant it would be necessary, in present day climatic conditions, to go at least as far north as latitude 60° S to find cirque glaciers eroding their basins at similar altitudes. Antarctica has been moving southwards during the Caenozoic[8]; assuming that the McMurdo Region has taken the shortest route southwards and has been moving at a steady rate of 20 cm/yr through 17° of latitude, the cirques would have last been in appropriate latitudes for cirque erosion 9.5 m.y. BP. Because 20 cm/yr is likely to be in excess of the maximum rate of movement and the movement may not have been in a straight line, the resulting Pliocene age for the cirques is an absolute minimum possible age.

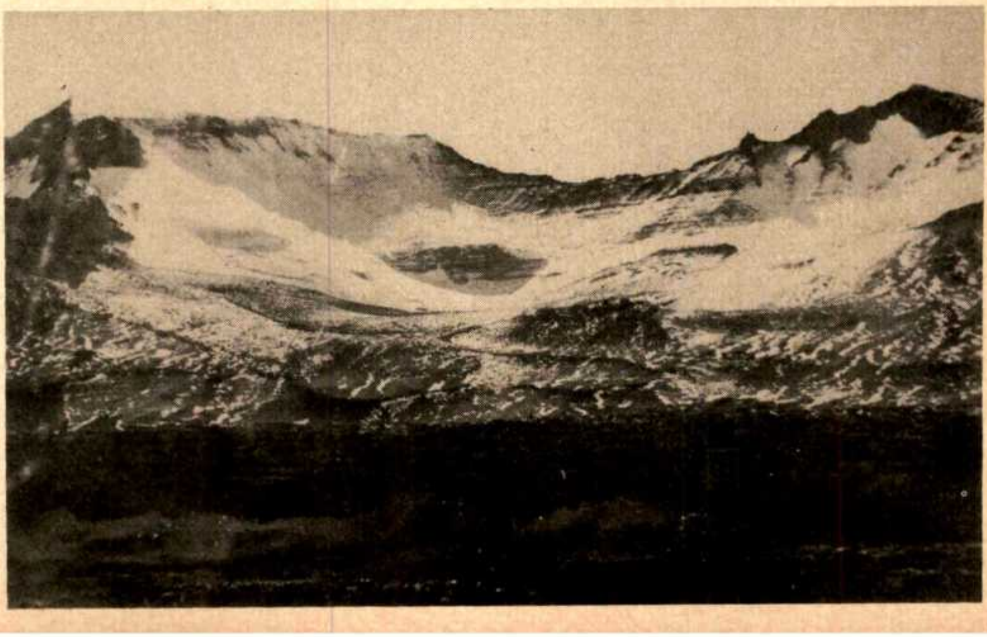

Fig. 1 Cirque above the north wall of the Wright Valley, Antarctica.

The best evidence available from palaeomagnetic data suggests that the McMurdo Oasis was last north of the Antarctic Circle at least 50 m.y. BP (ref. 9 and personal communication from D. A. Christoffel). This suggests that the alpine glaciation in which the McMurdo cirques may have been cut could actually be much older than 9.5 m.y. and could well have taken place in early or middle Tertiary times.

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Drag on Clusters of Submicron Spheres in Gravitational and Electrical Fields

THE dependence of hydraulic and aerodynamic drag on particle shape has been of interest for a considerable time but theoretical work has greatly exceeded experimental results, especially for submicron particles. Fuchs[1] gave a concise summary of the position and Preining[2] and Vomela and Whitby[3] have published mainly theoretical articles. Kunkel[4] determined the drag on various configurations of steel balls glued together and falling in oil, and Megaw and Wiffen[5] compared the diffusion coefficient of single and clustered submicron polystyrene spheres. Stöber *et al.*[6] deduced that the Stokes diameter d_n of a cluster containing n spheres should be related to the diameter d_1 of a single sphere by the expression

$$f_n = \frac{d_n}{d_1} \geq n^{\frac{1}{3}}$$

and confirmed its validity in an experiment in which single particles and clusters of submicron polystyrene spheres were centrifuged out of a spinning air stream. Stöber *et al.* also showed that, when expressed in terms of the Stokes diameter, Kunkel's results (in which the unit sphere was 0.12 cm diameter) agreed very well with those for submicron spheres in air.

The diffusion coefficient D (cm^2 s^{-1}) and the electrical mobility m (cm^2 V^{-1} s^{-1}) of a particle carrying charge e are related by the Einstein equation

$$D = \frac{299.8}{\mathrm{e}} \mathrm{k} T m$$

k being Boltzmann's constant and T the absolute temperature. For a spherical particle carrying a single electronic charge at 20° C, this reduces to $m = 39.6\ D$ and is much used by aerosol physicists. Megaw[7], pointing out that the diffusion coefficient is dependent on shape, said that it was not known whether the electrical mobility was dependent in the same way, and hence whether the Einstein relationship applied to non-spherical particles. The results given here show that it does not, and that the drag on a cluster of particles depends on whether the particle is moving in a gravitational or an electric field.

Table 1 Ratio, f_n, of Stokes Diameter of Singly Charged Clusters containing n Spheres and moving in an Electric Field to that of a Single Sphere

Unit sphere diameter (cm)	No. of spheres in cluster 2 f_2	3 f_3	4 f_4	5 f_5
1×10^{-5}	1.28	1.49		
1.6×10^{-5}	1.35			
2.2×10^{-5}	1.34			
3.3×10^{-5}	1.32	1.57	1.81	2.00
5.0×10^{-5}	1.31	1.58		
7.4×10^{-5}	1.29	1.55	1.79	
7.6×10^{-5}	1.28	1.56		
1.15×10^{-4}	1.29	1.57		

The experiments were performed using the mobility spectrometer described by us[8,9]. In this the aerosol is introduced as a narrow sheet midway between two parallel plates at equal and opposite potentials. Clean carrier gas flows through the instrument at the same speed as the velocity of introduction of the aerosol. Individual aerosol particles are carried across the gap between the plates and deposited on them at distances from the entrance inversely proportional to the electrical mobilities of the particles. If a monodisperse but coagulated aerosol at charge equilibrium is used, the particles are deposited on the plates in visible bands corresponding to singly, doubly, triply and so on charged singlets, and similarly charged doublets, triplets and so on. Fig. 1 is a photograph of the deposit on a plate, on the centre line of which a number of coated electron microscope grids were fixed before use to enable

Table 2 Comparison of Stokes Diameter Ratio, f_n, for Clusters in Gravitational Fields, Diffusing Clusters and Singly Charged Clusters in Electrical Fields

	Values of f_n Glued glass clusters falling in oil[4]	Magnetized steel clusters falling in glycerol *	Polystyrene clusters diffusing in air[5]	Magnetized steel clusters falling in syrup[6]	Polystyrene clusters centrifuged from air[6]	Singly charged clusters in an electric field
Diameter of unit sphere (cm)	0.12	0.159	8.8×10^{-6}	0.1 to 0.213	5.4×10^{-5} and 7.9×10^{-5}	1×10^{-5} to 1.15×10^{-4}
No. of spheres in cluster						
2	1.17	1.19	1.18	1.20	1.18	1.31
3	1.28	1.28	1.32	1.34	1.33	1.55
4		1.41		1.46	1.47	1.80
5		1.48	1.52	1.56	1.53	2.00
6	1.54			1.64	1.66	

* Unpublished results of Megaw.

positive identification of the bands to be made. Specimen photographs of the grids are also shown.

Table 3 Calculated Values of Electrical Mobility of Clusters

Diameter of unit sphere (μm)	No. in cluster	(i) Mobility ($cm^2 V^{-1} s^{-1}$) using Stöber's f_n values	(ii) Mobility ($cm^2 V^{-1} s^{-1}$) using Megaw and Wells's f_n values
0.1	2	1.98×10^{-4}	1.57×10^{-4}
	3	1.64×10^{-4}	1.22×10^{-4}
	4	1.41×10^{-4}	9.69×10^{-5}
	5	1.31×10^{-4}	8.28×10^{-5}
0.5	2	2.02×10^{-5}	1.71×10^{-5}
	3	1.78×10^{-5}	1.42×10^{-5}
	4	1.58×10^{-5}	1.20×10^{-5}
	5	1.50×10^{-5}	1.07×10^{-5}
1.0	2	9.03×10^{-6}	7.90×10^{-6}
	3	7.92×10^{-6}	6.58×10^{-6}
	4	6.93×10^{-6}	5.60×10^{-6}
	5	6.65×10^{-6}	5.00×10^{-6}

(i) Calculated from diffusion coefficient assuming Stöber's f_n values; (ii) as would be obtained by an electrical method assuming Megaw and Wells's f_n values.

By comparing the distances from the entrance at which particular clusters are deposited it is possible to determine the electrical mobility of each configuration and hence the value of its Stokes diameter (the diameter of the spherical particle having the same mobility as the cluster) using the theoretical expression derived by Fuchs and Stechkina[10]. The ratios f_2, f_3 and so on can then be determined.

The results for clusters made up of spheres of diameter 1×10^{-5} to 1.15×10^{-4} cm are given in Table 1. In Table 2 the values of f_n obtained by Kunkel[4] for glued clusters of glass spheres falling in oil, Megaw (unpublished work) for magnetized steel clusters falling in glycerol; Megaw and Wiffen[5] for submicron clusters of polystyrene spheres diffusing in air, Stöber *et al.*[6] for magnetized steel spheres falling in syrup and for micron sized clusters of polystyrene spheres centrifuged from air, are compared with the results of work described here. The f_n values for the electrically charged spheres differ considerably from the results for the other methods, which are in close agreement.

Megaw has noticed (unpublished work) that when asymmetric clusters of spheres are falling in a liquid the cluster takes up one of several preferred orientations. For example, doublets rarely fall in a vertical or horizontal mode but usually with the common axis inclined at about 60° to the vertical, and doublets which are released in the liquid in the vertical or

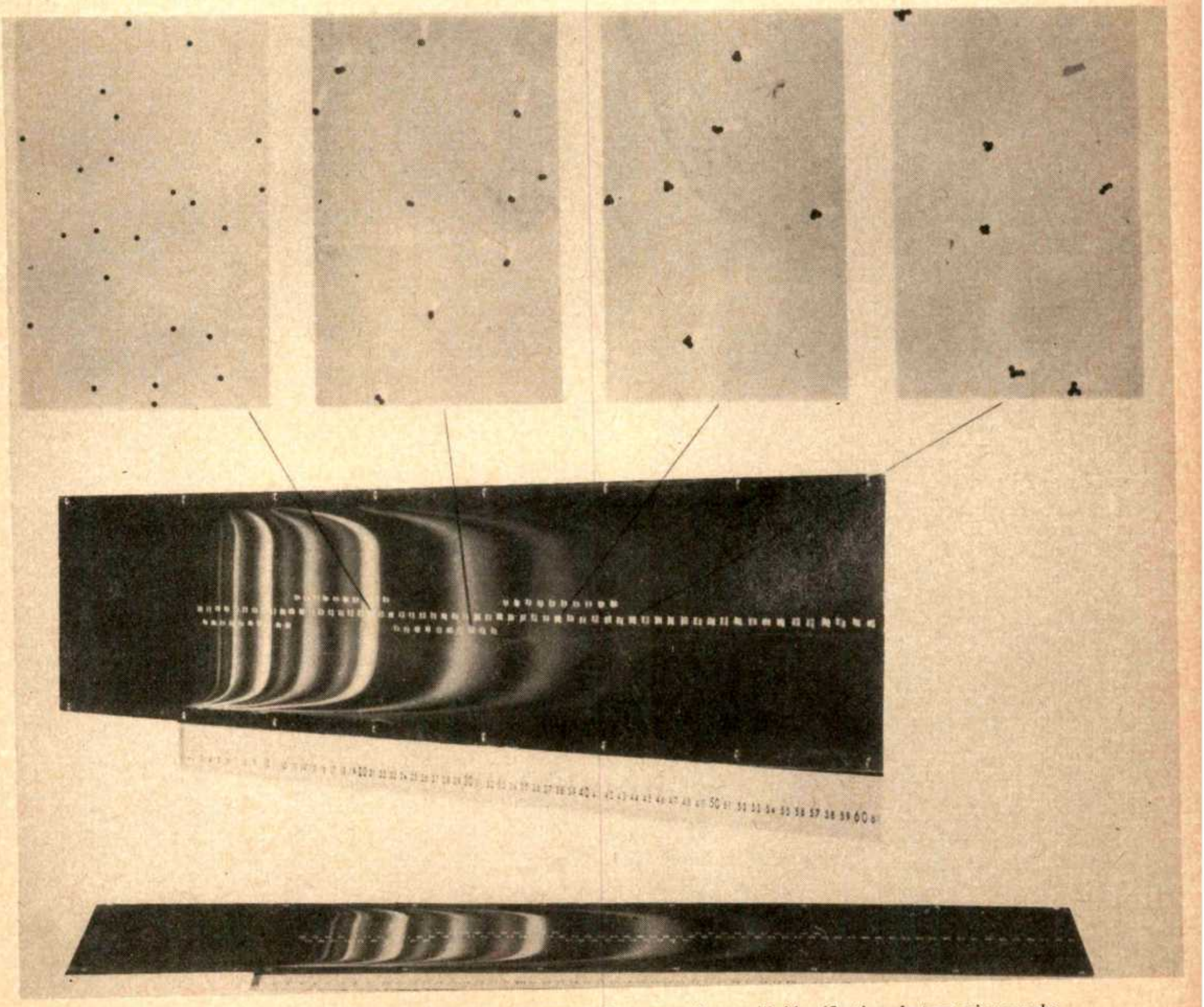

Fig. 1 Deposition bands of clusters of 0.33 μm diameter polystyrene spheres with identification electron micrographs.

horizontal mode generally turn quite quickly into the preferred orientation. More complex clusters appeared to have several preferred modes, one of which will nearly always be adopted irrespective of how the cluster is introduced into the fluid.

A single electronic charge, whether as an electron or singly charged small ion, attached to a spherical particle will not *per se* alter the drag in an electric field. However, a cluster carrying a single charge in an electric field will experience a couple which will change its orientation and hence its drag.

It follows that the equation $m = 39.6\ D$ relating the electrical mobility and diffusion coefficient cannot apply to non-spherical particles. The practical effect of this is illustrated in Table 3, where the electrical mobility calculated from the diffusion coefficient of clusters (using the f_n ratios of Stöber *et al.*) is compared with that which would be obtained by an electrical method. It appears that the electrical mobilities of clusters as calculated from the diffusion coefficient using the Einstein equation are from 20 to 60% greater than determined experimentally by an electrical method.

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Decomposition and the Determination of Fluorine in Biological Materials

THERE is considerable discrepancy in the published fluorine contents of some biological specimens[1-6] which can be at least partially attributed to shortcomings in standard decomposition techniques. We submitted a series of organofluorine compounds both to conventional decomposition[1-7] and to decomposition by pyrohydrolysis[8,9]; typical results are shown in Table 1*a*.

We found that acid digestion (compound 1) was almost ineffective in our conditions. Although the process of ashing with an additive in a covered platinum crucible is simple and satisfactory for inorganic fluorides (compound 5), it can lead to serious losses of organic fluorine through volatilization[10] (compounds 2 and 3). In the case of 'Teflon' (decomposition point 400° C) the loss of 6% fluorine is, however, probably due to the inability of the $MgO—O_2$ system to achieve a quantitative conversion of the strong C—F bond to fluoride ion even at 700° C. We overcame a similar difficulty in the elemental analysis of organofluorine compounds by applying MgO-catalyst additives at 900–1,000° C (refs. 11 and 12).

The pyrohydrolytic technique copes successfully with both organic and inorganic compounds, including CaF_2 and MgF_2. This method, suitably modified in the light of our experience (Fig. 1), makes use of a leak-proof piece of apparatus and combines in one operation the decomposition of sample and the evolution of hydrofluoric acid. Quantities of material varying from a few μg to a few g are placed in a platinum boat inside a quartz tube which is heated to 700–1,000° C (depending on compound and additive) in a moist current of oxygen or air. The combustion gases are swept through a layer of platinized silica wool maintained at 1,100° C and the hydrogen fluoride evolved is collected in water or dilute alkali. Mineral fluorides usually require an additive, for example V_2O_5 or WO_3. We established that silica, which usually interferes in fluorine determinations[1,2,13], is not detrimental in pyrohydrolysis (compound 6).

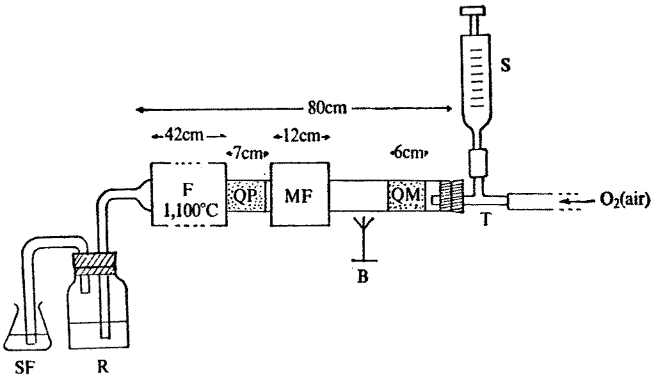

Fig. 1 S, Syringe for injecting distilled water through T-piece into silica wool plug, QM; B, gas burner; MF, movable furnace for heating sample (and additive); QP, plain silica wool to aid degradation of carbonaceous material[12]; F, furnace permanently maintained at 1,100° C; R, plastic receiver; SF, safety flask.

Table 1 Decomposition of Organofluorine Compounds

a Decomposition of model compounds

No.	Compound	Melting point (°C)	Fluorine observed (%)			Fluorine calculated (%)
			D	A	P	
1	m-Trifluoromethylbenzoic acid	—	2.1	—	29.9	30.0
2	Perfluoro-octanoic acid *	52	—	21.7	66.5	66.5
3	Trifluoroacetanilide	88	—	21.6	30.3	30.1
4	Teflon †	327	—	71.3	75.5	76.0
5	Sodium fluoride	—	—	45.2	45.3	45.2
6	Poly-3,3,3-trifluoro-n-propyl-methyl-siloxane	—	—	—	36.6	36.6

D, Digestion with 60% $HClO_4$ at 60° C for 15 h; A, ashing of a predried paste of compound and MgO, or Mg-succinate + LiOH, at 500° C for 24 h; P, pyrohydrolysis at 1,100° C; sample (and additive) at 700–1,000° C.

b Decomposition of biological materials

No.	Compound	Fluorine (p.p.m.)	
		Ce-alizarin complexan	Fluoride electrode
7	Darjeeling tea (Twining Blue Tips)		
	(i) Pyrohydrolysis (total fluorine)	104	99
	(ii) Pyrohydrolysis preceded by low temperature ashing (inorganic fluorine)	106	94
8	Lyons Quick Brew tea	128	107
9	Bournville cocoa	1.3	1.4
10	Freeze dried bacteria (*Escherichia coli*)	65	50
11	Clan tobacco	11	8
12	Ground human teeth	351	404

Pyrohydrolysis at 1,100° C; sample + V_2O_5 at 750–800° C; tube diameter 25 mm; injected water 30 cm³.
* Commercial product.
† Ashed at 700° C.

We determined fluorine spectrophotometrically as Ce(III)-alizarin-complexan[1,2,7,14] using an aqueous n-propanol solvent (unpublished results of J. M. Bather, D. B. Gordon and A. E. Tipping), and by direct electrode measurements with the ORION fluoride electrode[15,16]. The apparent discrepancy in the two sets of fluorine results for the biological materials in Table 1*b* can be traced back chiefly to the fluoride electrode and can be attributed to a marked difference in ionic strength between the unbuffered standard sodium fluoride solutions and the fluoride ion in the distillate from pyrohydrolysis. The higher ionic strength of the latter will tend to decrease the fluoride ion activity[15]. The opposite trend in the case of compound 12, which may indicate that some species in the distillate from teeth tend to interfere with the Belcher method, is being investigated further.

Samples of Darjeeling tea were subjected to decomposition by pyrohydrolysis (total fluorine) and also to low temperature ashing at 100–150° C followed by pyrohydrolysis (inorganic fluorine) in an attempt to distinguish between the two types of fluorine[3-6]. The low temperature asher (Tracerlab) allows the complete removal of organic matter because electromagnetically excited oxygen leaves the inorganic constituent undestroyed. The almost identical results for compound 7 (i) and (ii) indicate the absence of organic fluorine in tea, in agreement with Peters[7].

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BIOLOGICAL SCIENCES

Neutralization of Murine Mammary Tumour Virus by Sera of Women with Breast Cancer

MOUSE mammary tumour virus (MTV) causes breast cancer in mice. The mouse-MTV system is a useful model in the search for the hypothetical human mammary tumour virus (HMTV) causing the parallel disease in women. B particles similar in morphology to MTV were observed in negatively stained preparations of human milk by Moore *et al.*[1], and there seemed to be a connexion between the appearance of particles in the milk and the incidence of breast cancer among women.

It therefore seemed reasonable to explore the possibility of a close antigenic relationship between MTV and HMTV by means of cross-neutralization studies. Instances of such cross-antigenic relationships between viruses causing similar diseases in different species are known to exist. The familiar existence of smallpox–cowpox is a case in point. Human measles, canine distemper and bovine rinderpest form one of the several subgroups of myxoviruses in which various degrees of cross-neutralization have been demonstrated[2]. Similar cross-neutralization has been shown with the herpesviruses *H. hominis* (herpes simplex) and *H. simiae* (monkey B virus)[3]. Fink *et al.*[4] have reported data that suggest a degree of neutralization of a murine leukaemia virus (Rauscher) by sera of leukaemic patients. Data indicating the ability of sera from breast cancer patients to neutralize MTV are reported here.

In a preliminary experiment, MTV was neutralized by heterologous hyperimmune rabbit serum. Skim milk from the MTV-positive RIII mouse strain, containing approximately 10^5 ID_{50}/0.1 ml. at a dilution of 1 : 100, was incubated for 1 h at 37° C with ten-fold dilutions of antiserum. The preparation of the antiserum has been described already[5]. The virus–antiserum mixtures (0.1 ml.) were inoculated into C57BL mice and the infective status of the mice was determined by detection of viral antigen in the milk at the third lactation by the immunodiffusion assay of Charney *et al.*[5]. The presence of viral antigen in the milk at the third lactation is indicative of tumorigenesis[5,6]. The results obtained are summarized in Table 1. As expected, antigen detection in third lactation milk was eventually followed by tumorigenesis. Neutralization of the virus by the hyperimmune rabbit antiserum was substantially complete only at the highest antiserum level used (1 : 10 dilution).

As a result of the weak neutralizing capacity of the supposedly hyperimmune rabbit serum, modifications were made in the neutralization tests with human sera. Since RIII mouse milk contains much soluble (non-virion) viral antigen which might possibly interfere with the neutralization test, the MTV virions were purified by density gradient centrifugation by the method of Lyons and Moore[7]. The purified virion fraction, stored at $-90°$ C until use, contained approximately 10^4 ID_{50}/0.1 ml. Then 0.2 ml. of the purified MTV preparation was mixed with 1.8 ml. of serum, incubated for 1 h at 37° C and permitted to stand for 18 h at 4° C before inoculation of 0.1 ml. amounts into C57BL mice. The virus therefore contained approximately 100 ID_{50}/0.1 ml. at final dilution and the sera were practically undiluted. The five control sera from young adults were selected at random from the serum bank of the Philadelphia Department of Health. The description of these sera and the results obtained, as determined by the MTV assay, are given in Table 2. The mean incidence of MTV infection in mice inoculated with the control serum–virus mixtures was 87%, which is the usual incidence of antigen in third lactation milks of mice given fully infective doses of MTV[5]. The infectivity of the tumour sera–virus mixtures (mean = 69%) was lower in every case than those of the controls.

These data were analysed statistically. The difference between the control and tumour groups was significant (P= 0.02). Two of the tumour sera (H.G. and B.W.) were both significantly different from the control group (P=0.02) and a third (C.S.) was just short of significance (P=0.057). The 95% confidence intervals of the control and tumour groups barely interlock (control sera, 78.8%–95.4%; tumour sera, 57.9%–80.8%).

The presence of neutralizing antibodies in sera from human breast cancer patients and their absence from normal human sera indicates a viral aetiology for the human disease. It also indicates that the human and the murine viruses are closely related. Our results support the electron microscopic findings

Table 1 Neutralization of MTV by Heterologous (Rabbit) Anti-MTV Serum

Antiserum dilution	Infected mice* / Mice tested	% mice infected	Mice with tumours† / Mice tested	% mice with tumours
10^{-1}	1/15	7	1/14	7
10^{-2}	10/15	67	9/15	60
10^{-3}	8/15	53	8/15	53
10^{-4}	11/15	73	12/15	80
10^{-5}	11/14	79	10/12	83
10^{-6}	11/14	79	10/14	71
Control (no antiserum)	10/12	83	6/11	55

* Determined by MTV assay[5] at third lactation. † Mice observed for 18 months.

Table 2 Neutralization of Purified MTV by Sera from Women with Breast Cancer compared with Normal Controls

Serum	Interval to treatment*	Interval to serum†	Patient treatment	Age (yr)	MTV neutralization‡ Mice infected / Mice tested	% mice infected
C.S.	1 yr	8 yr	r.m., r-t.	85	9/13	79
E.M.W.	1 month	2 yr	r.m.	60	7/10	70
H.G.	3 months	5 yr	Excision	76	9/14	64
B.W.	1 yr	4 months	r-t.	36	9/14	64
M.B.G.	3 weeks	5 yr	r.m.	55	9/11	82
			Breast cancer sera, totals		43/62	69.3
A.B.	Normal serum control				10/12	83
J.L.	,,				11/12	92
S.M.	,,				12/14	86
B.G.	,,				14/16	88
J.S.	,,				7/8	88
			Control sera, totals		54/62	87.0

r.m., radical mastectomy; r-t., radiotherapy.
* Duration of symptoms before medical treatment.
† Interval from time of treatment to time serum was drawn.
‡ Determined by MTV assay[5].

of Moore *et al.*[1] of B particles in human milk which are morphologically identical with mouse MTV.

Further neutralization studies of human breast cancer sera obtained from patients at various stages of the disease are being done using control non-tumour sera and tumour sera from patients with tumours other than breast cancer paired for age and sex.

The cross-antigenic relationship between MTV and HMTV indicated in this study suggests that MTV could be used to render women immune to breast cancer. This would require that antisera to MTV and HMTV be reciprocally cross-neutralizing, that is, antibody to MTV must also neutralize HMTV. Experimental techniques to demonstrate this do not exist at present.

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Localizing ^{3}H-GABA in Nerve Terminals of Rat Cerebral Cortex by Electron Microscopic Autoradiography

CONSIDERABLE biochemical, physiological and pharmacological evidence supports the idea that GABA is an important inhibitory neurotransmitter substance in the mammalian central nervous system (CNS)[1-3]. Cytochemical techniques for demonstrating the cellular location of this amino-acid in the CNS have so far not been available.

Slices and synaptosomes from rat cerebral cortex will actively accumulate ^{3}H-GABA when incubated *in vitro*[4]. After briefly incubating with ^{3}H-GABA, the unchanged amino-acid is concentrated in the tissue without any significant accumulation of labelled metabolites. Furthermore, the radioactive GABA can be released by electrical stimulation from cortical slices[5], and it has a subcellular distribution closely similar to that of the endogenous amino acid[6]. This labelling technique, in combination with autoradiographic procedures, therefore offers a potential method for the localization of GABA-containing structures in the CNS. Such an approach has recently been applied to the localization of ^{3}H-GABA at the light microscope level in slices of rat cerebellar cortex[7] and rabbit retina[8]. We now present preliminary results obtained by electron microscope autoradiography which indicate that ^{3}H-GABA is predominantly accumulated by nerve terminals in rat cerebral cortex.

Small slices of rat cortex were incubated with ^{3}H-GABA as previously described[4]. The concentration of ^{3}H-GABA in the incubation medium was 5 μM (10 μCi/ml.; 2,3-^{3}H-GABA, specific activity 2.0 Ci/mmol, New England Nuclear Corp.) and the incubations were performed at 25° C for 10–30 min. Some experiments were also performed with samples of rat cortex homogenates prepared in isotonic sucrose, and incubated in Krebs phosphate solution with labelled GABA as we have described. At the end of the incubation with ^{3}H-GABA, the labelled medium was discarded (after centrifugation of homogenate samples), and the tissue slices or homogenate pellets were washed with ice-cold medium, and then fixed by the addition of fresh medium containing glutaraldehyde. In preliminary experiments, using these uptake conditions, tissue extracts were subjected to ion exchange chromatography or paper chromatography[4]. ^{3}H-GABA accounted for 95±9% of the total radioactivity in both slices and homogenate pellets (mean±s.e.m. of three experiments), and ^{3}H-GABA was the only labelled compound detected by paper chromatography. We have also determined the extent of retention of ^{3}H-GABA in the tissue samples after fixation, by dissolving tissue samples and determining their radioactivity after various fixation procedures. These results (Table 1) indicate that almost two thirds of the labelled GABA was retained after fixation with glutaraldehyde. For autoradiographic studies, the fixed samples were treated with osmium tetroxide, dehydrated in ethanol and embedded in epoxy resin.

Table 1 Effect of Fixation Conditions on Retention of ^{3}H-GABA

Fixative	% retention of ^{3}H-GABA
3% potassium permanganate	17.8 (n=2)
5% glutaraldehyde	65.2±4.1 (n=4) (±s.e.m.)

Cortical homogenates were incubated with ^{3}H-GABA as described in the text; at the end of the incubation, the homogenate was centrifuged, and the radioactivity present in the pellet was determined after solubilization overnight with NCS solubilizer (Searle). Fixatives were added to other labelled pellets obtained from the same homogenate, and after standing for 40 min at 4° C the fixative solution was removed, the pellets rinsed and solubilized for counting. All fixative solutions were made up in the incubation medium (Krebs phosphate solution). Results are expressed as percentages of the amount of ^{3}H-GABA present in unfixed samples, and are mean values of n experiments.

Autoradiographs were first prepared using tissue sections of 1–2 μm thickness, in order to evaluate the overall distribution of radioactivity. The samples were dipped in Ilford L-4 emulsion and developed with DK 170 developer (Kodak) after exposure periods of 5–15 days. Examination by light microscopy showed intense autoradiographic activity over the cortical slices and homogenate pellets. In cortical slices the radioactivity was restricted to the neuropil, with a notable absence of silver grains over the cell bodies of the large cortical neurones. There was no obvious localization of ^{3}H-GABA within the layers of the cortex. We have now used very small slices prepared with a mechanical chopper, so that the conditions of the autoradiographic study are very similar to those used in previous biochemical studies[4,6]. It seems likely that slices prepared in this way are not the most suitable for determining the cytological localization of ^{3}H-GABA by light microscopy. Our primary objective, however, was to determine the cellular location of ^{3}H-GABA uptake sites at high resolution by electron microscopy, rather than to examine the morphological distribution of such uptake sites in the tissue.

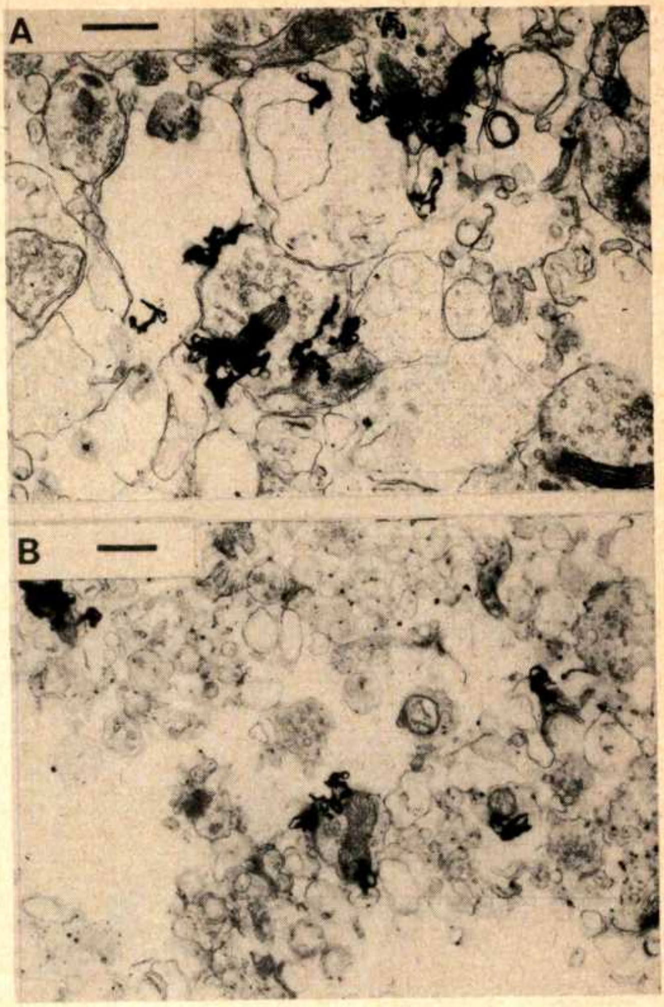

Fig. 1 Electron microscope autoradiographs of tissue samples incubated in ^{3}H-GABA as described in the text. Regardless of whether the tissue samples were slices (*A*) or homogenates (*B*), the predominant site of autoradiographic activity as indicated by the presence of irregular, electron-dense silver coils was over nerve terminals. Clusters of 8–10 grains as seen over the nerve terminals in *A* were never seen over any other structural element except nerve terminals. The calibration bar represents 0.5 μm.

For electron microscope autoradiography, thin sections (80–100 nm) of the same tissue blocks were placed on celloidin coated slides, stained with lead citrate and lightly coated by carbon evaporation before dipping in dilute Ilford L-4 emulsion to obtain a monolayer of silver halide crystals. After exposures of 9–21 days, development in D 19B (Kodak) revealed autoradiographic activity over nerve terminals in both cortical slices and homogenates (Fig. 1). The distribution of silver grains was quantitatively analysed in randomly oriented low magnification micrographs of cortical slices. The results (Table 2) showed a highly significant localization of the radioactive GABA to nerve terminals and preterminal unmyelinated axons. These tissue components accounted for an average of 38±3% of total section area (5 samples of 275 μm^2), but contained 82±1% of all silver grains in the same sections. In sections of the pellets obtained after the labelling of cortical homogenates with ^{3}H-GABA *in vitro*, there was again an almost exclusive localization of autoradiographic activity in nerve terminals, with little or no labelling of other components such as free mitochondria or myelin fragments (Fig. 1).

We have estimated the proportion of nerve terminals which contained ^{3}H-GABA in cortical slices and homogenates. These results (Table 3) show a remarkable agreement between the estimates obtained in slices and homogenates after various periods of autoradiographic exposure. There was no significant difference between the proportion of labelled terminals after various exposure times, which suggests that all labelled

Table 2 Localization of ^{3}H-GABA in Slices of Rat Cerebral Cortex

Tissue component	Mean percentage of surface area occupied *	Mean percentage of total silver grains †
Glial cells	13.0 ± 1.1	2.1 ± 0.1
Neurone cell bodies + dendrites	38.9 ± 3.0	11.3 ± 1.8
Nerve terminals	23.5 ± 3.6	70.7 ± 2.3
Myelinated axons	5.0 ± 1.7	1.0 ± 0.05
Unmyelinated axons	14.5 ± 1.3	11.2 ± 1.5
Unidentified and extracellular space	5.3 ± 1.1	3.2 ± 1.1

* Percentage of total area occupied by various tissue components was estimated by application of a 220 point grid to randomly selected low power electron micrographs of cortical tissue. The area of tissue in each micrograph was 275 μm^2, and the results are means ± s.e. for five analyses.

† The distribution of silver grains was analysed in the same electron micrographs; results are expressed as the mean percentages (± s.e.) of total grain population in each micrograph located over the various tissue components.

terminals were estimated even after relatively short exposure times. The only difference observed between exposure times of 9, 15, and 21 days was that the number of silver grains over each nerve terminal increased with the longer exposures. After the 21 day exposure, the median number of silver grains over each labelled terminal in cortical slices was two, with some large terminals giving rise to as many as eight to ten grains.

Table 3 Percentage of Nerve Terminals containing ^{3}H-GABA in Slices and Homogenates of Rat Cerebral Cortex

Sample and exposure time (days)	Mean percentage of labelled terminals ± s.e.m.	Total No. of terminals analysed	No. of micrographs analysed
Cortical slices:			
9	27.0 ± 2.4	556	12
15	26.6 ± 1.3	232	5
21	27.2 ± 3.0	679	13
Cortical homogenates:			
9	22.0 ± 2.1	218	7
15	28.4 ± 2.9	214	7
21	29.6 ± 2.3	242	7

Mean results for analyses of five to thirteen autoradiographs of cortical slices or homogenates, each containing forty to fifty nerve terminals.

The similarity between the estimates obtained from cortical slices (27% labelled terminals) and homogenates (28–30% labelled terminals) also suggests that the incubation of small cortical slices *in vitro* leads to an adequate labelling of all the GABA uptake sites. If one assumes that GABA uptake sites are associated with the nerve terminals which contain endogenous GABA, then our results suggest that such terminals account for about 30% of all synaptic terminals in the rat cerebral cortex. This conclusion is in accord with other evidence which suggests that GABA is the principal inhibitory neurotransmitter in the mammalian cerebral cortex[1-3].

These preliminary findings indicate that the use of radioactively labelled GABA in conjunction with electron microscope autoradiography will be useful for future studies of the distribution and fine structure of GABA-containing elements in the CNS. Autoradiographic studies at the light microscope level have already provided information on the distribution of such structures in the cerebellum and retina[7,8]. The analysis of labelled nerve terminals in brain homogenates may make it possible to arrive at an accurate estimate of the relative abundance of GABA terminals in various regions of the brain and spinal cord. The technique may also be applicable to other amino-acids for which a transmitter role has been proposed. We are grateful to Drs P. Orkand and E. Kravitz for personal communication of their results.

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Preparation of Highly Radioactive Bovine Anti-mouse Lymphocyte Antibody

FOR use in humans the active components of anti-lymphocytic serum (ALS) must be sufficiently free of irrelevant substances, concentrated and non-toxic for it to be injected intravenously. With this in mind earlier investigations designed in the context of an experimental model[1] were aimed at (1) preparing pure anti-lymphocytic antibody (ALSAb) from anti-lymphocytic globulin preparations (ALG) and (2) increasing the biological activity of such preparations by labelling the protein in them with a low energy gamma-emitting isotope (^{125}I). It was hoped that the specifically localized irradiation would play a role in incapacitating the target lymphocytes[1]. ALS raised in rabbits is widely used, but many workers have reported considerable variation in the quality of ALS from individual rabbits. It would therefore be advantageous to raise ALS in larger animals such as cattle or pigs so that larger pools of material could be obtained. The earlier experiments with ALSAb prepared from rabbit ALS have been extended in the experiments described here, in which the effectiveness of purified bovine anti-mouse lymphocyte antibody (BALSAb) and ^{125}I-BALSAb has been measured. A preliminary investigation has also been made of the possibility of using a column of thymocytes bound to 'Sepharose', for the preparation of BALSAb.

The ALS was raised by injecting a 2 month old Jersey calf in several sites with Freund's complete adjuvant containing 4×10^{10} heat treated thymocytes (49° C, 20 min). A second injection of 3×10^{10} cells, not in adjuvant, was given after 14 days and the calf was bled a week later[2]. The median survival time (MST) of this serum, measured by the standard method used in this laboratory[3], was 27 days. Anti-lymphocyte globulins (ALG) were prepared from ALS by precipitation in half-saturated ammonium sulphate (4° C), followed by ion-exchange chromatography (Whatman DE 32) using 0.02 M Sorensen phosphate buffer containing 0.02 M NaCl. ALSAb was prepared from ALG by a batch procedure using one of the methods described previously[1]. Briefly, washed thymus cells in Gey's solution were fixed for 3–4 min in 0.125% glutaraldehyde. After washing, the cells were incubated with normal bovine gamma globulin and then washed by suspending them in 0.1 M acetic acid (*p*H 3.1) followed immediately by centrifugation (5 min at 600*g*). After rapid adjustment of the *p*H to 7 the cells were washed three times in Gey's solution containing 0.1% bovine serum albumin. These "precycled" cells were then used for the batch preparation of ALSAb by adding 1 μg

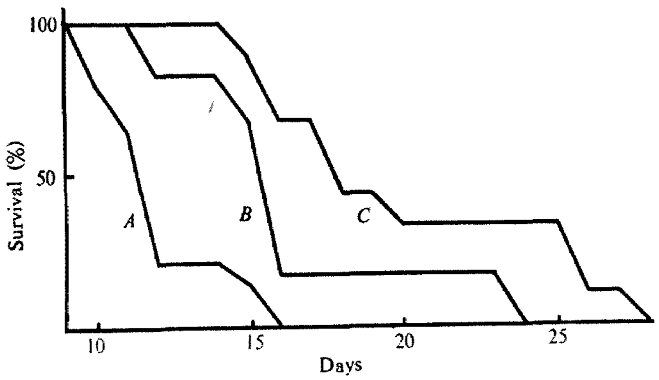

Fig. 1 The survival of A strain tail skin grafted onto CBA male mice. *A* is a group of fourteen untreated controls; *B* is a group of seven mice injected intravenously with 250 µg BALSAb 4 h after grafting; *C* is similar to *B* except that the BALSAb was labelled with ^{125}I (3.2 µCi/µg), and there were ten mice in the group. The horizontal axis is days after grafting.

ALG for every 1×10^6 cells, incubating them at 20° C for 10–15 min, washing three times with Gey's solution, eluting antibody with acid (*p*H 3.1), rapidly adjusting the *p*H of both eluate and cells to 7, followed by three more washes of the cells before the start of the next cycle. Up to ten elution cycles can be completed before a significant drop in the yield of ALSAb results. Each eluate was concentrated using 'Aquacide' (Calbiochem) and cytotoxic titres were then measured using ^{51}Cr-labelled lymphocytes by the method of Ruszkiewicz[4]. The eluates were pooled after it was found that they all had specific activities at least ten-fold greater than the starting material. The pool of eluted material was tested for all components of bovine serum by immunoelectrophoresis. Only globulins with a γ_2 mobility were detected in the BALSAb preparation. BALSAb was labelled with ^{125}I by the chloramine-T method[5] using radioisotope 5 supplied by the Radiochemical Centre, Amersham (IMS 3).

Three groups of male CBA mice aged 3–4 months were grafted with A strain tail skin[4]. Four hours later two groups were injected intravenously with either 250 µg of BALSAb or 250 µg of ^{125}I-BALSAb (3.2 µCi/µg). Fig. 1 shows that unlabelled BALSAb prolongs the life of test skin grafts and that the labelled material shows a somewhat greater prolongation effect than the unlabelled material, confirming earlier results with rabbit ALSAb[1].

In an attempt to develop an easier procedure for preparing ALSAb than the "batch" method, a column of fixed thymocytes conjugated to 'Sepharose' was prepared. About 10^{10} thymocytes (outbred mouse) were fixed as described earlier and suspended in borate buffer (0.01 M boric acid, 0.025 M Na borate, 0.075 M NaCl, *p*H 8.4). 'Sepharose 2B' (400 µg, Pharmacia) was prepared for conjugation as described by Porath *et al.*[6], except that the protein used in their procedure was replaced by fixed thymocytes. The acid wash before use of the 'Sepharose' conjugate as an immunoadsorbent was made on the column after adding 25 mg of normal bovine gamma globulin. For the preparation of BALSAb 10 mg of ALG was added to the column which was then washed with borate buffer until there was no detectable protein in the effluent. The acid elution step was made by passing 0.25 M acetic acid through the column. The absorbance of the effluent was monitored by an LKB Uvicord (240 nm) and the *p*H was monitored with indicator papers. Two different fractions were obtained, one with the *p*H of the effluent steady at 3 and the other after borate buffer had been reapplied to the column and at a time when the *p*H of the effluent was rising (Fig. 2). Table 1 shows that there is no difference in the specific activity of the two fractions, and moreover that the specific activity of these BALSAb fractions is about ten-fold greater than acid-treated starting material (BALG–acid). BALSAb eluted from the column was exposed to similar degrees of acidity and temperature for about 30 min. Table 1 also shows clearly that the untreated starting material (BALG–control) has a cytotoxic titre eight-fold higher than the BALG–acid (15 min at *p*H 3.1–3.0, 20° C). The relatively greater success of the batch method may well be due to the short time during which the antibody is kept at *p*H 3. A certain amount of denaturation of antibody by acid may be an explanation of the significant content of IgG without antibody activity, observed previously[1] in ALSAb prepared by the batch method. Denaturation of anti-peptide antibodies kept for 1 h in similar conditions of acidity has been reported[7]. Bachvaroff *et al.*[8] successfully prepared a purified cytotoxic antibody against thymocytes using a batch method, but they did not include any data on the stability of this antibody in acid conditions (*p*H 2.5, 0° C, HCl-glycine buffer). Others have noted the lability of ALS in acid conditions[9,10], and Woodruff and his colleagues have shown that acid-treated ALG loses its ability to prolong survival of skin allografts[11].

Table 1 Cytotoxic Activity of ALS Antibody eluted from a Column of Thymocyte-'Sepharose' Conjugate

Material	Cytotoxic end point (µg of protein)	Relative cytotoxic titre	Yield (µg)	Relative cytotoxic activity as a factor of: BALG-acid	BALG-control
BALSAb-A	0.34	8.4	285	9.3	1.1
BALSAb-B	0.30	9.8	500	10.9	1.3
BALG–acid treatment	3.1	0.9	—	—	0.12
BALG–control	0.38	7.7	—	8.2	—
Standard (see ref. 1)	2.9	1.0	—	—	—
BALSAb from batch preparation	0.05	58.0	—	—	—

Total yield of gamma globulin (OD_{280}) in the BALSAb cuts is about 0.8 mg from 30 mg BALG (2.6%). The yield for batch preparations ranged from 2.5–3.5%.

$$\text{Relative cytotoxic titre} = \frac{\text{µg standard needed to lyse 50\% of target cells}}{\text{µg experimental sample needed to lyse 50\% of target cells}}$$

It seems reasonable to conclude that the ability of bovine ALS antibody to prolong skin grafts can be increased by labelling the material with ^{125}I. The practicality of preparing BALSAb using a column of insoluble immunoadsorbent seems to be limited at the moment by the marked lability of ALS antibody in acid conditions.

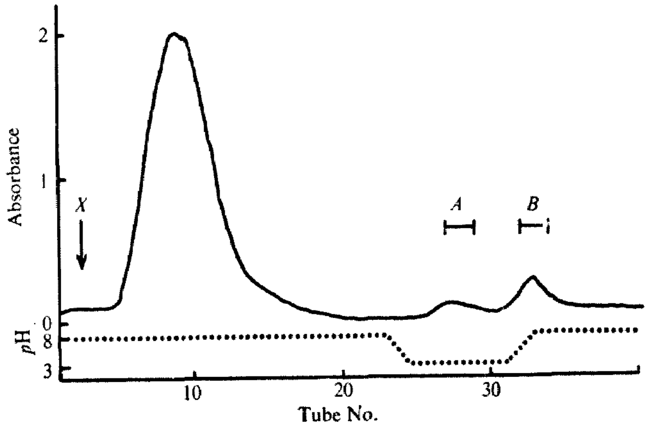

Fig. 2 The effluent from a column (2 cm diameter × 5 cm) of 400 mg 'Sepharose'/10^{10} thymocytes to which 10 mg of bovine ALG had been added at *X* monitored by an LKB Uvicord at 240 nm. The column was washed with borate buffer and acid elution was with 0.25 M acetic acid. Seven ml. fractions were made at a rate of 12–14/h. The dotted line indicates the *p*H of the effluent. See Table 1 for further information about cuts *A* and *B*.

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In vitro Assay of Cell Mediated Immunity in Human Cancer: Definition of Leukocyte Migration Inhibitory Factor

SEVERAL studies have implicated the delayed hypersensitivity reaction in the body's response to cancer. Hughes and Lytton found that one cancer patient in four demonstrated a delayed cutaneous hypersensitivity response to an antigen consisting of small cytoplasmic particles obtained after ultrasonic disruption of their tumours[1]. There have been several studies of the ability of cancer patients to react to the antigens commonly used for delayed cutaneous hypersensitivity testing[2-9]; in general, while responsiveness was affected little, if at all, in patients with early cancer, it decreased as disease and debility progressed. The ability to develop contact sensitivity to dinitrochloro-benzene or dinitrofluoro-benzene is decreased in cancer patients, particularly those with advanced disease[10,11]. Such sensitivity has been shown to be related to prognosis[12].

George and Vaughan proposed the use of *in vitro* cell migration to study delayed hypersensitivity[13], and the mechanism was further defined by Bloom and Bennett[14]. They noted that interaction between lymphocytes from tuberculin-hypersensitive guinea-pigs and *p*-phenylenediamine (PPD) resulted in the formation of a substance which inhibited migration of normal peritoneal-exudate cells. Søberg and Bendixen[15,16] showed that the brucella antigen inhibited migration of leukocytes obtained from individuals with positive skin tests only. Falk *et al.*[17] sensitized volunteers with homologous skin grafts after which migration of the sensitized lymphocytes was inhibited by antigens from the skin graft donor.

It seemed from these studies that human tumours might either contain or produce a substance which inhibits migration of the patient's lymphocytes. If this substance were the migration inhibitory component of the hypersensitivity reaction, its demonstration by this test would also imply prior sensitization of the peripheral leukocytes.

Human tumour and normal tissue were either minced with scissors and incubated in Eagle's medium (containing 100,000 U of penicillin G, 400 U of streptomycin and 50 mg each of oxytetracycline and chlortetracycline/l.) for 24 h or disintegrated with ultrasound. The larger cell fragments were cleared from the medium by centrifugation for 10 min at 2,000*g*. When tests were run to ascertain the effect of continued presence of tumour on leukocyte migration, samples of media were removed before centrifugation. Leukocytes were obtained from blood drawn in heparinized syringes, the erythrocytes were allowed to settle out, and the plasma and leukocytes were transferred to centrifuge tubes. Plasma was removed by centrifugation at 750*g* for 4 min, and the leukocytes were washed three times with 5% dextrose lactated Ringer and resuspended in an equal volume of Eagle's medium. Ten-lambda siliconized capillary tubes (Drummond) were filled with the suspension, sealed with 'Permoplast' clay, and centrifuged to separate the cells and medium. Finally, the capillary tubes were broken at the leukocyte medium interface before incubation. Stained smears of the leukocytes so prepared revealed about 60% lymphocytes, 40% polymorphonuclear leukocytes, and a few erythrocytes.

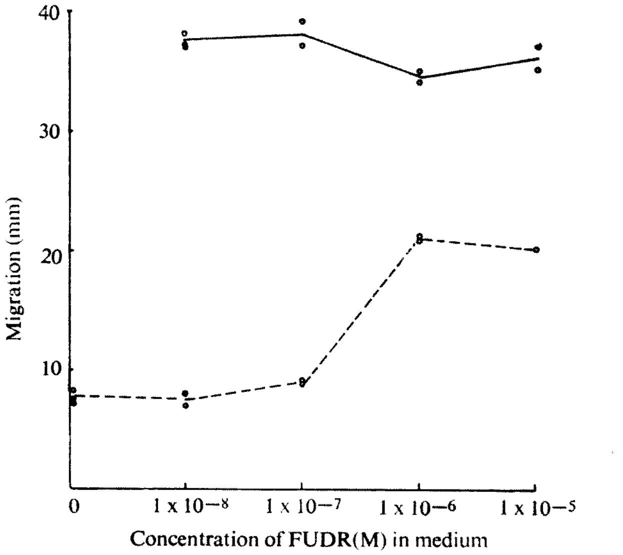

Fig. 1 Effect of 5-fluorodeoxyuridine (FUDR) in partially reversing inhibition of leukocyte migration produced by phytohaemagglutinin. ○—○, FUDR; ○ - - - ○, FUDR + phytohaemagglutinin.

The solution derived from the tumour was drawn to fill the tips of siliconized Pasteur pipettes, and the portion of the capillary tube containing leukocytes was inserted into the tip of the Pasteur pipette. The tip of the Pasteur pipette containing the "antigen" solution and the leukocytes in the capillary tube was sealed with Permoplast clay and broken off. The open end was sealed with Dow Corning stopcock grease, and the distance of leukocyte migration along the pipette was determined after 24 h incubation at 37° C.

Most of the tumours liberated into the medium a substance which inhibited migration of the patient's leukocytes (Table 1). Inhibition of migration was no greater with continued presence of tumour cells in the medium than when the cells had been removed before testing for migration. Migration was also inhibited by ultrasonicates of the tumour. Medium which inhibited migration of a patient's leukocytes had no effect on normal leukocyte migration (Table 2). It was possible to distinguish between inhibition of migration resulting from blastogenesis and that resulting from specific migration inhibitory factors by adding 5-fluorodeoxyuridine to the medium at the time of the test. When phytohaemagglutinin (0.04 ml./ml. of medium) was present in the medium, migration did not occur. Partial reversal of this inhibition occurred when blastogenesis was blocked by 5-fluorodeoxyuridine in concentrations greater than 1×10^{-7} M (Fig. 1). Although the inhibition of migration caused by photohaemagglutinin

Table 1 Inhibition of Autologous Leukocyte Migration by Cancer

Patient	State of tumour preparation	% inhibition of migration $\frac{\text{control-tumour}}{\text{control}} \times 100$	Significance of difference of migration tumour versus control (P)	Tumour specimen
1	Cell free	48	<0.01	Breast carcinoma
2	Cells	41	<0.01	Breast carcinoma
	Cell free	24	0.05	
3	Cells	38	<0.01	Breast carcinoma
	Cell free	28	<0.50, >0.10	
4	Cell free	23	<0.01	Breast carcinoma
	Cell free + FUDR	14	<0.01	
5	Cell free	15	<0.10, >0.05	Breast carcinoma
	Ultrasonic	22	<0.02, >0.01	
6	Cells	79	<0.01	Bronchogenic carcinoma
7	Cells	8	>0.50	Bronchogenic carcinoma
	Cell free	19	<0.05, >0.02	
8	Cells	9	>0.50	Bronchogenic carcinoma
	Cell free	25	<0.10, >0.05	In hilar lymph node
9	Cells	44	<0.01	Carcinoma of maxillary sinus
	Cell free	63	<0.01	
10	Cells	6	>0.50	Colon carcinoma
	Cell free	21	<0.50, >0.10	
11	Cell free	(12)	<0.50, >0.10	Colon carcinoma
	Ultrasonic	17	<0.01	
12	Cell free	33	<0.01	Gastric carcinoma
	Cell free + FUDR	39	<0.01	
13	Cell free	26	<0.02, >0.01	Ovarian carcinoma
14	Cells	36	<0.01	Rectal carcinoma,
	Cell free	15	<0.50, >0.10	Perineal recurrence
15	Cell free	62	<0.01	Squamous of parotid
	Cell free + FUDR	58	<0.01	
16	Cell free	28	<0.01	Thyroid carcinoma

Inhibition of leukocyte migration produced *in vitro* by elements of autologous tumour. Tumour was presented to the leukocytes in Eagle's medium in one of three forms: as the supernatant present after incubation of a tumour mince for 24 h, as the same preparation from which the cells had been removed by centrifugation, or as the ultrasonicate of the tumour. These are denoted in Table 1 as cells, cell free and ultrasonic, respectively. 5-Fluorodeoxyuridine (FUDR) was added to the medium in a concentration of 1×10^{-5} M when noted.

could be attributed partly to an effect associated with blastogenesis, such was not the case with human tumours (Table 1: tumours 4, 12 and 15).

These results show that human cancers either contain or produce a substance which inhibits *in vitro* migration of leukocytes obtained from the individual in whom the tumour arose. Our findings with cancer are similar to results obtained after HL-A antigen sensitization[17]. Falk *et al.* found that inhibition of lymphocyte migration was proportional to the HL-A antigen difference between graft donor and recipient. In relating extent of malignant disease to inhibition of leukocyte migration, we found that of five breast cancer patients the one with the most advanced disease demonstrated the greatest inhibition of leukocyte migration. Although we cannot yet relate our findings to prognosis, it is possible that elaboration of a sensitizing tumour substance which prevents tumour–lymphocyte interaction may be detrimental. Such a situation may explain the paradox noted by Hellström *et al.* that lymphocytes from patients with tumours are capable of destroying autochthonous neoplastic cells *in vitro*[18]. Systemic release of such a substance could cause generalized reduction of lymphocyte migration and explain the decreased responsiveness of advanced cancer patients to delayed cutaneous hypersensitivity-type antigens or to sensitization to dinitrochloro-benzene. The partial reversal by 5-fluorodeoxyuridine of inhibition of leukocyte migration may also explain the observation of Blomgren *et al.* that fluorinated pyrimidine chemotherapy enhanced the delayed cutaneous hypersensitivity response in advanced cancer patients[19].

These findings raise the possibility that delayed hypersensitivity operates as a defence mechanism early in the natural history of cancer but that as the cancer becomes more advanced certain components of the reaction, specifically inhibition of leukocyte migration, become detrimental.

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Table 2 Comparison of Autologous and Homologous Leukocyte Migration

Source of leukocytes	Type of patient's tissue Normal	Tumour
Patient 5	0.55 ± 0.08 (8)	0.47 ± 0.05 (7)
Control	0.38 ± 0.03 (6)	0.40 ± 0.03 (6)
Patient 11	0.25 ± 0.03 (5)	0.28 ± 0.02 (5)
Control	0.25 ± 0.00 (3)	0.28 ± 0.02 (3)
Patient 13	0.38 ± 0.04 (6)	0.28 ± 0.05 (5)
Control	0.31 ± 0.09 (2)	0.29 ± 0.06 (3)

Mean migration (cm) ± s.d. (number of replicates) of leukocytes in cell free medium in which either tumour or normal tissue had previously been incubated for 24 h. Leukocytes were obtained from either the tumour-bearing patient or from controls without tumour.

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Lentinan, a New Immuno-accelerator of Cell-mediated Responses

BCG is almost the only agent now used as the immuno-accelerator of cell-mediated responses[1-3], but it has various biological side effects and a complicated chemical structure, so that it is not necessarily the most suitable agent. We reported that lentinan[4,5] and pachymaran[6] strongly inhibited the growth of transplanted tumours in mice, and these two polysaccharides are worth considering as excellent immuno-accelerators.

Table 1 Effect of Neonatal Thymectomy (TX) on Antitumour Activity of Lentinan

Mice	Sample	Dose	Body weight change	Average weight of tumour	Inhibition ratio	Complete regression
Normal mice	Lentinan	1 mg/kg × 10	+2.3 g	0.1 g	99.6%	9/10
	Control		+2.4 g	10.3 g		0/10
TX mice	Lentinan	1 mg/kg × 10	+1.6 g	7.3 g	6.4%	0/5
	Control		+2.8 g	7.8 g		0/5

Table 2 Effect of Antilymphocyte Serum (ALS) on Antitumour Activity of Lentinan

Sample	Dose	Body weight change	Average weight of tumour	D/A	Inhibition ratio	Complete regression
Lentinan	1 mg/kg × 10	+8.1 g	0.2 g	1/7	98.6%	5/7
ALS+ lentinan	1 mg/kg × 10 0.1 ml. × 10	+1.6 g	5.8 g	1/8	43.4%	0/8
ALS	0.1 ml. × 10	+1.0 g	8.5 g	1/7	16.7%	0/7
NRS+ lentinan	0.1 ml. × 10 1 mg/kg × 10	+4.8 g	2.4 g	3/5	76.7%	2/6
Control		+4.3 g	10.2 g	0/8		0/8

The antitumour effect of lentinan is lost in neonatal thymectomized mice, and decreased considerably by administration of antilymphocyte serum (ALS). SWM/MS mice were thymectomized by the method of Sjodin *et al.*[7] within 48 h of birth. After 6 weeks, 0.05 ml. (about 6×10^6 cells) of 7 day old sarcoma 180 ascites tumour was transplanted subcutaneously into the right groin of the TX mice (body weight 21–23 g), and from the following day 1 mg/kg of lentinan was injected intraperitoneally daily for 10 days. Five weeks after transplantation, the tumours were removed and their weights were compared with those of untreated control thymectomized mice to give the inhibition ratio. Table 1 shows the results and the antitumour activity of lentinan on normal mice. In normal mice, the tumour inhibition ratio of lentinan was 99.6% and regressed tumours completely in nine out of ten cases, but in TX mice the inhibition ratio was 6.4% and no tumours regressed.

Antilymphocyte serum (ALS) was prepared in Japanese white rabbits using mesenteric lymph node of SWM/MS mice as antigen[8]. As in the previous experiment, sarcoma 180 cells were transplanted subcutaneously in the SWM/MS mice and, from 24 h onwards, 1 mg/kg of lentinan and 0.1 ml. of ALS were injected intraperitoneally once a day for 10 days. Comparison of the tumour weight 5 weeks after transplantation with that of untreated control mice showed that the strong antitumour effect of lentinan was markedly reduced by ALS (Table 2).

ALS has a selective immunosuppressive effect[9-13] and is said to suppress especially cell-mediated immune responses, having little influence on humoral immune responses. According to Miller[14] and Waksman *et al.*[15-17], selective depletion of thymus-derived circulating small lymphocytes and loss of cell-mediated responses have been recognized in neonatal thymectomized mice. The fact that lentinan does not cause the regression of a tumour graft in thymectomized mice and is compensated by the administration of ALS indicates that the mode of action of lentinan is part of the thymus-derived immune mechanism, in which small lymphocytes, play an important part. This is a reasonable explanation of the suggestion that regression of a tumour caused by lentinan is the result of stimulation of cell-mediated responses, so that lentinan will provide an effective reagent for cellular immunology. Further studies on the influences of lentinan in other cell-mediated responses, such as homograft rejection and delayed type hypersensitivity, are in progress. We have no evidence that lentinan enhances the production of humoral antibody.

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Private and Public Antigens of the Mouse H-2 System

It was observed rather early in the history of the mouse histocompatibility-2 (H-2) system that some antigens of the system are limited to only one or very few H-2 alleles, whereas others are shared by several alleles[1]. Antigens with limited distribution were called "private", as opposed to "general" antigens present in many different H-2 alleles[2]. It has been tacitly assumed that the distinction between private and general antigens (the latter will be called "public" here) is an artificial one and that the difference between them would disappear when new strains and new H-2 alleles were analysed. This, however, proved not to be the case. So far H-2 alleles of some seventy strains and stocks have been determined, and the distinction into private and public antigens still holds. It can be argued, of course, that because most of the strains of the laboratory mouse are related to each other in their origin[3], the differences in frequencies of individual H-2 antigens are still only apparent.

It was therefore unexpected that during the H-2 typing of wild mice, almost all of the mice reacted very strongly with most of the antisera against public antigens but only very few reacted with antisera against the private antigens[4]. It could still have been argued that because the sample of wild mice was collected at only four different locations and because mice from the same locality showed conspicuous homogeneity in their H-2 phenotypes, the difference was again a mere reflexion of the relatedness of the mice in the sample. To clarify this point, another sample of 100 wild mice from twenty different localities in the Ann Arbor area was collected and tested.

Mice were trapped alive in Sherman traps in granaries, barns and corn cribs on farms at least 5 km beyond the city limits and usually at least 2 km apart. On a few farms, however, mice were captured at several different localities usually not more than 50 m apart. The red blood cells of the captured mice were tested with a battery of H-2 antisera of restricted reactivity (Table 1) in a direct haemagglutination test in polyvinyl-pyrrolidone (PVP)[5]. Only strong high-titred antisera were selected for this study.

The phenotypic frequencies of the twelve H-2 antigens tested for are shown in Table 2. The antigens can be clearly divided into two groups: those present in 75–95% of the localities where mice were trapped, and those present in only 0–10% of the localities. The first group—the public antigens—consists of antigens H-2.1, 3, 5, 6 and 8. These are the same antigens which are widely shared by the alleles of the laboratory mouse[6]. The second group—the private antigens—consists of antigens H-2.2, 4, 9, 17, 19, 23 and 24. The presence of these antigens in the H-2 chart of the laboratory mouse is in most cases

Table 1 Antisera Used for the Typing of Wild Mice

Code designation	Antiserum made in: Strain	Antiserum made in: H-2 allele	Immunizing tissue supplied by: Strain	Immunizing tissue supplied by: H-2 allele	Antibodies present
C-1 *	(C3H.SW × B10.M)F_1	b/f	C3H.NB	p	1,16
S-12	(B10.D2 × A)F_1	d/a	HTH	h	2
C-3 *	(A.BY × WB)F_1	b/w	A.SW	s	3,19
S-29	(A.BY × AKR.M)F_1	b/m	A	a	4
S-46	(B10.D2 × HTG)F_1	d/g	B10	b	5,33 ?
S-35	C3H	k/k	C3H.R3	r	6,18 ?
S-48	(B10 × A.SW)F_1	b/s	A.CA	f	8,9
S-22	(B10.A × A.SW)F_1	a/s	A.CA	f	9
S-21	(C3H.B10 × AKR.M)F_1	b/m	C3H.Q	q	17
S-24	(B10 × A)F_1	b/a	A.SW	s	19,7 ?
C-23 *	(B10 × LP.RIII)F_1	b/r	B10.BR	k	23,32
S-34	(B10.Y × C3H.B10)F_1	p/b	I	l	24

* Antisera supplied by Transplantation Immunology Branch, National Institutes of Health, Bethesda, Maryland.

Table 2 Frequencies of Positive Reactions of Wild Mice Red Blood Cells with Antisera against Individual H-2 Antigens

Localities	H-2 antigens 1	2	3	4	5	6	8	9	17	19	23	24
KPA †	5/8 *	0/8	4/8	0/8	6/8	4/8	1/8	0/8	3/8	0/8	0/8	0/8
KPB	7/8	0/8	4/8	0/8	7/8	1/8	0/8	0/8	0/8	0/8	0/8	0/8
KPC	10/11	8/11	6/11	0/11	11/11	3/11	2/11	0/11	0/11	0/11	0/11	0/11
STA	5/5	0/5	4/5	0/5	5/5	5/5	2/5	0/5	0/5	4/5	0/5	0/5
STB	4/5	0/5	4/5	0/5	5/5	3/5	2/5	0/5	0/5	0/5	0/5	0/5
STC	0/4	4/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4	0/4
BUA	3/3	0/3	1/3	0/3	3/3	2/3	1/3	0/3	0/3	0/3	0/3	0/3
BUB	3/3	0/3	0/3	0/3	3/3	3/3	0/3	0/3	0/3	0/3	0/3	0/3
CHA	2/2	0/2	1/2	0/2	2/2	1/2	2/2	0/2	0/2	0/2	0/2	0/2
CHB	2/3	0/3	1/3	0/3	3/3	1/3	1/3	0/3	0/3	0/3	0/3	0/3
WOA	3/4	0/4	2/4	0/4	4/4	4/4	2/4	0/4	0/4	0/4	0/4	2/4
GAA	6/8	0/8	3/8	0/8	6/8	7/8	0/8	0/8	0/8	0/8	0/8	0/8
PTA	3/3	0/3	2/3	0/3	3/3	1/3	1/3	0/3	0/3	0/3	0/3	0/3
DRA	3/4	0/4	4/4	0/4	3/4	4/4	2/4	0/4	0/4	0/4	0/4	0/4
WAA	2/3	0/3	0/3	0/3	2/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3
WRA	1/2	0/2	1/2	0/2	2/2	2/2	2/2	0/2	0/2	0/2	0/2	0/2
DIA	1/1	0/1	0/1	0/1	1/1	0/1	1/1	0/1	0/1	1/1	0/1	0/1
KEA	5/8	0/8	3/8	0/8	5/8	6/8	6/8	0/8	0/8	0/8	0/8	0/8
SAA	7/7	0/7	3/8	0/7	7/7	5/7	4/7	0/7	0/7	0/7	0/7	0/7
SAB	2/8	0/8	5/8	0/8	2/8	2/8	3/8	0/8	0/8	0/8	0/8	0/8
Total	74/100	12/100	48/100	0/100	80/100	54/100	32/100	0/100	3/100	5/100	0/100	2/100
Positive localities (%)	95	10	80	< 1	95	85	75	< 1	5	10	< 1	5

* Number of positive mice over total number of mice tested.

† The same first letters indicate the same farm.

Table 3 *In vivo* Absorption of Antiserum S-46 (anti-H-2.5, 33?) in Wild Mice

Absorbed in	Reaction with test cells of WRA67	WAA64	DRA62	BUA17	BUA16	PTA53	CHA51	CHA2	STA34	STA39	A	B10.D2
BUA19	0	0	0	0	tr	1	3	2	1	4	2	0
CHA26	0	0	0	0	0	1	0	0	0	1	tr	0
WOA26	0	0	0	0	0	0	0	0	0	2	0	0
KPA58	0	0	0	0	0	2	2	1	1	4	0	0
PTA52	0	0	0	0	0	0	2	2	3	4	0	0
DRA63	0	0	0	0	0	0	0	0	0	tr	0	0
WAA65	0	0	0	0	0	0	3	2	2	3	0	0
WRA66	0	0	0	0	0	0	0	0	0	0	0	0
DIA68	0	tr	0	0	0	0	0	0	0	0	0	0
B10.D2	3	3	3	2	3	3	3	3	3	3	3	0
B10	0	0	0	0	0	0	0	0	0	0	0	0
B10.A	0	0	0	0	0	0	0	0	0	0	0	0

0 and tr, negative reaction; 1 and 2, weakly positive reaction; 3 and 4, strongly positive reaction in haemagglutination test.

limited to one H-2 allele and alleles derived from it by recombination[6]. Antigen H-2.23 is a new antigen defined by antiserum (B10 × LP.RIII)F_1 anti-B10.BR and is limited to allele $H\text{-}2^{k}$ and its recombinational derivatives[10]. Antigen H-2.24 is also a new antigen, defined by antiserum (B10.Y × C3H.B10)F_1 anti-I/St and limited to alleles $H\text{-}2^{j}$ and $H\text{-}2^{i}$ (J. Klein and D. C. Shreffler, unpublished results). Three of the private antigens, H-2.4, H-2.9 and H-2.23, were absent from the tested sample. (A few weakly positive reactions with antisera against these antigens proved to be non-specific in repeated tests and/or in absorption *in vivo*.) Non-specific agglutinability of mouse red blood cells in the PVP technique is not a rare phenomenon, however; and so it could be argued that some H-2 antisera tend to react nonspecifically with erythrocytes of wild mice more often than others, thus providing the basis for what seems to be two groups of antigens, public and private.

To test this possibility absorption analyses were performed (Table 3). Antiserum S-46, which according to present knowledge should contain only two antibodies, anti-H-2.5 and anti-H-2.33, was injected intraperitoneally into wild mice (0.2 or 0.3 ml. per mouse) which were previously typed as H-2.5 positive in the direct haemagglutination test. The injected mice were bled 4–24 h later and absorbed sera were tested by the PVP haemagglutination test against other (untreated) H-2.5 positive wild mice and control inbred strains. (Although the antiserum was made against B10 tissue, usually it does not react with B10 erythrocytes, so A erythrocytes were used instead.) The wild mice in the sample can be divided into two groups according to their ability to absorb antiserum S-46: (1) those which absorb the antiserum completely, both for other H-2.5 positive wild mice and the H-2.5 positive inbred strain; and (2) those which even after absorption for 24 h leave some activity in the serum against cells from some H-2.5 positive wild mice, while at the same time clearing the serum completely for others. Absorption of antiserum S-46 in B10.A ($H\text{-}2^{a}$) mice removes activity against the cells of all the wild mice, indicating that the residual reaction after absorption in the second group of wild mice is not a consequence of anti H-2.33 in the antiserum (allele $H\text{-}2^{a}$ is H-2.33 negative). Normal sera collected from the wild mice before the absorption do not agglutinate erythrocytes of any wild mice; the residual reaction in the second group must therefore be specific and cannot be caused by natural antibodies normally present in the sera of some wild mice, and also present in the sera collected after *in vivo* absorption.

Two conclusions can be drawn from the absorption experiment. First, the reaction of most, if not all, the wild mice with antiserum S-46 in the direct haemagglutination test is specific, for all the mice typed as S-46-positive in the direct test were also able to absorb the antiserum *in vivo*. Second, there is some indication that antiserum S-46 contains more than one antibody and that, perhaps, the antigen H-2.5 is divisible into subtypes. The second point, however, requires more attention and will be studied further, both genetically and immunologically. Absorption experiments with other antisera were also performed; the details of these will be presented elsewhere. Basically they confirm the distribution and frequencies of the individual H-2 antigens as presented in Table 2. The conclusion seems therefore to be unavoidable that the phenomenon of public versus private H-2 antigens is real and not an artefact of limited knowledge of the H-2 polymorphism.

Several important observations pertinent to the phenomenon of private and public antigens may be made. First, the number of known private H-2 antigens is constantly growing[7], while the number of public antigens has remained practically the same since 1954. Second, genetic factors controlling the private H-2 antigens seem to be located at the extreme ends of the H-2 region, while factors controlling the public antigens seem to be centred around the *Ss* locus[8,12]. Third, private H-2 antigens form two series, and members of the same series are mutually exclusive[8]; no such exclusiveness has yet been observed for the public antigens. Fourth, genetic factors for at least some of the public antigens appear to be located on both sides of the *Ss* locus; this observation is interpreted as evidence for duplications within the H-2 region[9,12]. No evidence for duplications of factors for private antigens has so far been presented. Fifth, extensive serological analysis of some public antigens (H-2.1 and H-2.3) provided evidence that they are divisible into several subtypes or "families" of antigens[10,11]; no subtypes have yet been described for any private antigens.

The difference between public and private antigens can be explained on the basis of Shreffler's duplication model of the H-2 region[12], with the following minor modifications: it is postulated that there are only two genes for private antigens, one at each end of the region, and that these genes are relatively unrelated to each other and to the rest of the region. There is virtually no cross-reactivity between the products of these genes and the products of the rest of the region. The public antigens, on the other hand, are controlled by a series of genes which arose by duplications around the *Ss* locus. There are only slight antigenic differences between the products of individual genes in this series, and there is therefore extensive cross-reactivity between them. In the natural population, one detects not only the antigen against which a given antiserum was originally made but also its subtypes. This leads to much higher frequencies of positive reactions than with antisera against private antigens.

It has been pointed out that there is a close homology between the mouse H-2 and the human HL-A systems[8]. It should be stressed, however, that this homology does not include the public antigens of the H-2 system, for there is no clear evidence for the existence of similar antigens in the HL-A system. But it is possible—as has happened so often before—that the example set by the H-2 studies will soon be followed by similar observations in the HL-A system. It is very likely that antisera against public antigens of the HL-A system—if such antigens in this system exist—are discarded as too complex and therefore unsuitable for serological analysis.

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Does Virus Infection have Evolutionary Significance?

ANDERSON's theory[1] that "evolution depends largely" on the transfer of genetic material by viral transduction may be plausible for microbes, but in cellular organisms there are some serious objections.

First, the argument that susceptibility to viral infection must have a selective advantage because organisms do not have the complete resistance which they could evolve is equally valid for susceptibility to bacterial infections, parasites and even predators. That an organism has not reached an imagined "perfection" is insufficient reason to impute a function to the existing "imperfection".

Second, it is improbable that the "interchange of genes 'on approval' " would promote parallel evolution in cellular organisms to any significant degree, because of the integration of genotypes (coadaptation)[2]. It is unlikely that an alien gene or block of genes will perform well in a genetic environment with which it has never had any previous interaction.

The author's parliamentary analogy falls on the same point. Populations harbour vast amounts of genetic variation[3-5]. Thus to be closer to reality, the analogy should be to a parliament with a vast library of variant versions of laws, nearly all of which are being tried out constantly, in a country where many statutes interlock. An entirely new statute would have little chance of being compatible with the pre-existing complex system and would almost certainly cause chaos if it were introduced even in a somewhat altered form. The question is whether there is any "need" for entirely new statutes while the vast library of variants exists.

In this connexion, Anderson supposes that "plants and animals which are free from virus infection would evolve very slowly if at all". I suggest that the important kind of variation for evolutionary change is that exemplified by isozymes[3,4], as well as by concealed recessives detected in *Drosophila*[5], and that this sort of variation is abundant in nature. The very recently published evidence of a similarly large variation in *Limulus*[6], an animal long thought to have had an extraordinarily stable evolutionary history, further argues against any simple relationship between the amount of genetic variation and the speed of evolution.

My last and most serious objection concerns the mechanism by which cellular organisms would evolve susceptibility to virus infection. Anderson believes that the selective advantage of infectability is in allowing novel genes to be taken in and tried out. A novel gene would have to increase the reproductive success of the host and also have to be incorporated into the host's germ cell line if genes for susceptibility are to increase in frequency in the host population. If the expression of the novel gene did not increase the fitness of the individual into which it was transferred but only that of some descendant, then there would be no selection at the level of the individual and no increase in genes for susceptibility. The only mechanism left would be group selection, a tenuous hypothesis of doubtful validity[7].

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Hangover Effect of Hypnotics in Man

DRUGS used to induce sleep—the hypnotics—are among the most widely used of all medicaments. It has been estimated that "At a very rough reckoning about one night's sleep in every ten in Britain is hypnotic-induced"[1]. This assertion stems from the number of prescriptions each year for barbiturate (20 million) and non-barbiturate hypnotics (5 million)[1,2] and emphasizes the importance of studying the detailed clinical pharmacology of such drugs. But so far there has been little attention to the residual or hangover effect detectable the next morning. Significant impairment of performance on a battery of psychological tests was found up to 15 h after a hypnotic dose (200 mg) of chlorpromazine or quinalbarbitone given at night[3]. Similarly, behavioural impairment and electroencephalographic changes have been reported 12 h or more after nitrazepam or amylobarbitone sodium[4]. In these studies, however, subjects were forbidden caffeine-containing drinks for the period of the study and were thus undergoing some degree of caffeine withdrawal.

We have investigated the hangover effects of two hypnotics each given in two doses compared with a placebo: butobarbitone sodium (100 and 200 mg) and nitrazepam (5 and 10 mg), a new non-barbiturate hypnotic, which is widely used and safe in overdoses[5]. Ten normal subjects each received all five treatments (placebo, and two drugs in two doses) at weekly intervals as part of a fully balanced design, using double blind procedures. They were told not to drink alcohol on the evenings when they took the sleeping tablets but were allowed their normal intake of caffeine-containing beverages both night and morning. The drug was taken at 23.00 h and the physiological and psychological tests included the electroencephalogram both at rest and during an auditory reaction time task, and palmar sweat gland activity. Psychological tests included key-tapping rate (a measure of simple motor speed), the digit symbol substitution test (a measure of coding and associative skills) and linear scales (100 mm) on which the subjects rated themselves for quality of sleep the previous night and feeling of alertness at the time of testing.

Many tests were affected significantly by the drugs. For example, tapping was slowed from a mean of 377 taps per min after the placebo to 344 per min after 200 mg of butobarbitone sodium ($P<0.001$, Fig. 1). Auditory reaction time was prolonged from a mean of 219 ms after the placebo to 247 after 200 mg of butobarbitone ($P<0.001$). Fewer items of the digit symbol substitution test were completed, for example the mean was 76 in 90 s after the placebo and 70 after 10 mg of nitrazepam ($P<0.001$). These effects were chiefly a consequence of motor impairment, for performance times were proportionately increased much more than were errors. Subjectively, quality of sleep was generally improved by the drugs but alertness at the time of testing was diminished after only the larger doses (Fig. 2).

The electroencephalogram was analysed by dividing it into four broad wave bands using analogue filters. Significant drug-induced changes were found in the energy levels of each wave band. In general, energy in the slow wave bands (2.4–4.0 Hz; 4.0–7.5 Hz) was decreased and that in the faster bands (7.5–13.5 Hz; 13.5–26.0 Hz) increased. For example, the proportion of fast wave activity (13.5–26.0 Hz) was increased by both drugs and this variable proved very sensitive to drug effects (Fig. 3).

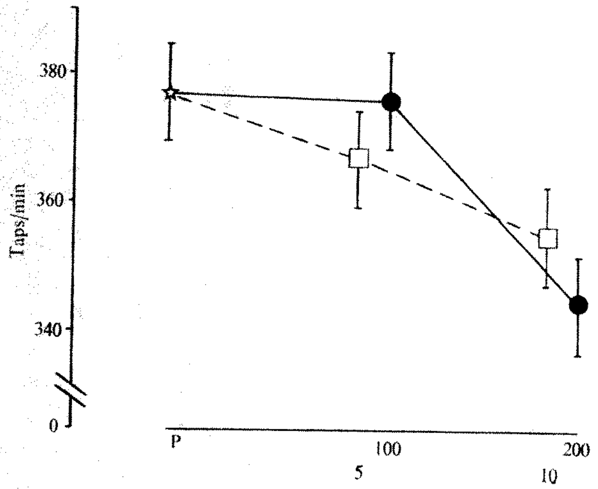

Fig. 1 Effects of hypnotics the following morning on tapping rate. The means and standard errors for ten normal subjects are shown for placebo (★), butobarbitone sodium (●, 100 and 200 mg), and nitrazepam (□, 5 and 10 mg).

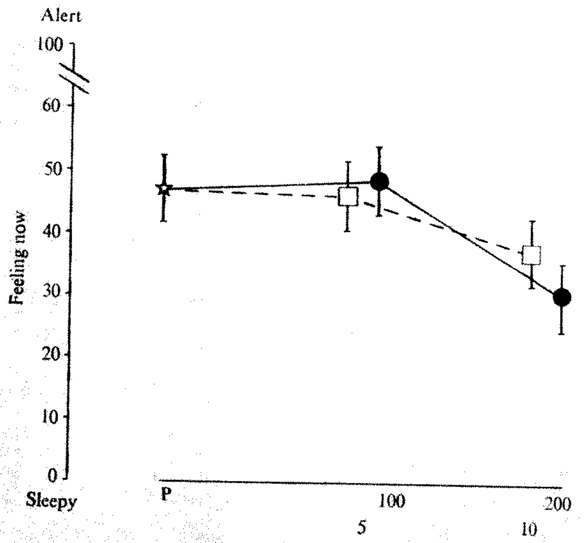

Fig. 2 Effects of hypnotics the following morning on rating of subjective feelings of alertness. The ordinate scale is in terms of mm from the "sleepy" end of the linear scale. Symbols as in Fig. 1.

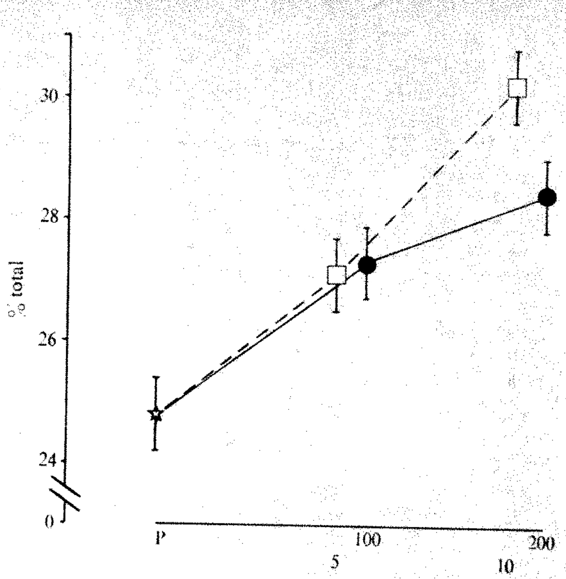

Fig. 3 Effects of hypnotics the following morning on the 13.5–26.0 Hz wave band of the electroencephalogram. The mean rectified voltage in this wave band is expressed as a percentage of that of the entire electroencephalogram. Symbols as in Fig. 1.

Thus definite hangover effects are demonstrable 12 h after hypnotic doses of a barbiturate and a new, widely used, non-barbiturate hypnotic. These effects are consistent with the pharmacokinetics of these drugs: nitrazepam, for example, has a half life of 6–10 h[6].

The doses used were in the recommended clinical range. Our study with a small number of normal subjects gave some indication of the magnitude of effects to be expected. Caffeine was not withdrawn because such deprivation changes drug status. Our results indicate that a normal intake of caffeine does not counteract the appreciable hangover effects of hypnotics; it is not known what an increased amount of caffeine would do. It is difficult to extrapolate from normal subjects to patients suffering from persistent insomnia, as sleep deprivation itself may impair performance the next morning. Nevertheless test performance after the worst night's sleep (self rating) was superior to that following satisfactory sleep with a hypnotic. It is hoped eventually to investigate the chronic use of hypnotics in insomniac patients in whom the processes of cumulation and tolerance might have counteracting effects. Meanwhile we must remain aware that, although these hypnotics lessen the distress of the insomniac patient, psychological impairment and electrophysiological changes are inevitably left the next morning. Indeed, it is unrealistic to expect any adequate hypnotic drug to be devoid of pharmacological effects on wakening.

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BOOK REVIEWS

Lancashire Hot-pot

University Perspectives. By John Knapp, Michael Swanton and F. R. Jevons. Pp. x+297. (Manchester University: Manchester; Barnes and Noble: New York, November 1970.) £3.00.

FOR roughly the last quarter of the nineteenth century, the precursors of the universities of Leeds, Liverpool and Manchester were combined as constituent parts of the Victoria University. It must have been a very loose federation because each college was sustained by fierce local pride, and, in retrospect, dissolution of the alliance seems inevitable. It took place as soon as it decently could after the demise of the Good Queen and Manchester was left with its own university. It is unique amongst English universities outside Oxford, Cambridge and London in consisting of two parts still affectionately called "Owens" and "Tech" by many former students. The latter is now the University of Manchester Institute of Science and Technology (UMIST) and for sixty-five years it has been the Faculty of Technology of the University of Manchester, though it has been called successively the Municipal School of Technology and the Manchester College of Science and Technology; names which emphasized its difference from the University of Manchester. Even now, many departments in UMIST are duplicated in Owens and to the outsider they seem often to operate as two independent institutions.

Mancunians will also claim that the University of Manchester has always held primacy of place amongst the great civic universities, and even a Yorkshire reviewer will concede this to be true for almost all the first half of this century. Many factors contributed to this. The city of Manchester was the centre of a great conurbation which, through its trade, looked outwards, and which possessed vigorous industries frequently founded by European immigrants who brought with them a love of music, literature and art and, encouraged by the *Manchester Guardian*, the city developed a real belief in itself as the country's pacemaker in the sciences and humanities, and in its university as one of its chief instruments of progress. Those who doubt this should read Mary Stocks's *My Commonplace Book*, where the impressions made on a Londoner by Manchester and its university are made abundantly clear. Immigrant scholars, scientists and engineers were made welcome and much esteemed in the university and, aided by its Literary and Philosophical Society with its glorious links with Dalton and Joule, the university encouraged the interested citizenry of Manchester to know what its savants were about and to share in their successes. Its science departments were especially distinguished; it was naturally expected in Manchester that professors in physics and organic chemistry, if not Nobel laureates already, would, in due course, be so honoured. Perhaps the most important factor in the success of the university was that the academic staff numbers were not incomprehensibly large; Alexander the philosopher could and did talk with Rutherford the physicist.

With UMIST, Manchester University is now the largest of the civic universities, and indeed exceeds both Oxford and Cambridge in size. But, as one who loves, admires and occasionally despairs of civic universities, I have not perceived that it has maintained its former pre-eminence. Partly this is due to the fact that the other universities have begun to catch up, partly that "formula financing" which has necessarily underlain much of UGC thinking in the last decade is a powerful force towards uniformity of university levels, but partly, as the editors of this book clearly feel, because the social unit comprehensible to a staff member in Manchester is now the department, and that outside the narrow professional context, communication, both intra- and extramurally, is often non-existent or ineffective. This book consists of twenty essays by Manchester academics aimed at reducing this unprofitable isolation. Inevitably it is a pot-pourri lacking the consistency of quality of ingredients of a good hot-pot. But unevenness is interesting and the variety of styles gives unparalleled insights into Liam Hudson's convergent and divergent minds. It is invidious to select but I must report that I found the essays on government and history extremely interesting—that on history takes the form of a conversation about the Manchester history school involving Tom Jones, Thwackum and Square—whereas that on economics is arid and dull and does little justice to the distinguished work carried out in this field in Manchester. The last essay is by a theologian and in many ways is also the best because it is almost the only one, apart from Professor Cox's on English, which recognizes that many young people now at universities are seeking meaning and purpose in their lives. Sad to relate, many go away with minds full of tribology and marginal costs or orbital symmetries or whatever, but with little awareness of their own identity. Perhaps the theological essay serves to remind us all that possibly university teachers only have an incentive to think about their subjects in a wider context when their subjects become sufficiently unpopular! Meanwhile, horizons of Owens and Tech academics could be broadened by reading *University Perspectives*, and I suspect that this would also apply to many readers of *Nature*.

F. S. DAINTON

Contemporary Marxism

Marx and Contemporary Scientific Thought. (Publications of the International Social Science Council, No. 13.) Pp. xi+612. (Mouton: The Hague and Paris, 1969.) 89 francs.

THREE years ago this May in Paris, while students battled with police in the streets, a distinguished group of forty-five scholars from twenty-one nations took part in a symposium on "The Role of Karl Marx in the Development of Contemporary Scientific Thought". I suspect that, for many years to come, historians will be smiling over this coincidental unity of theory and practice.

In the meantime, it is good to have at last the collected proceedings of this conference. I should perhaps offer two preliminary warnings about the book. The first is that about half of the essays have been written in or translated into French. Because some of the translated material was originally composed in rather complex German, it is clear that a fair reading knowledge of the French language will be required. Second, *Marx and Contemporary Scientific Thought* scarcely touches upon theoretical and/or experimental developments in the natural sciences. "Scientific thought" in this instance relates almost exclusively to the social sciences.

Despite those two provisos, I hope that this bulky volume will attract a certain portion of *Nature*'s audience. For the work crystallizes out a set of theoretical tendencies potentially as important to social scientists as the May Days were to young revolutionaries. I refer here to the first major re-evaluation of Marxist social theory since the 1930s. Interestingly enough, the leading theorists behind this reorientation were themselves students and young lecturers shortly before the Second World War. Since that time, Marx's writings have served them not as an orthodoxy but as an essential point of departure. Thus three leaders of the new movement—Adorno, Habermas and Marcuse—while subscribing to Marxism in general terms, have felt free to alter Marx's concepts of, for example, revolution and the labour theory of value.

The outline of the neo-Marxist synthesis is only now emerging, perhaps because many of its practitioners, such as Eric Hobsbawm, are historians who have regularly eschewed the role of theoretical sociologist. In his essay for the work under review, Hobsbawm does attempt to explain the ideological presuppositions behind his own work. The end result, however, is less the synthesis of a new view than the destruction of several prevailing ones. As an example of theory building of considerable power, Jürgen Habermas's piece on "Technique et Science comme 'Ideologie'" should be consulted.

Whatever may be said about the direction of the "new Marxism", it is evident that it stands little chance of becoming the new Communist orthodoxy within the foreseeable future. To judge from the papers presented by the Russians at the Paris conference, the wave of the present in Eastern Europe is iconography, not iconoclasm.

PAUL GARY WERSKEY

Fine Fare

Synthetic Food. By Magnus Pyke. Pp. viii + 145. (John Murray: London, December 1970.) £2.25.

WE know, or think we know, all the essential components of an adequate diet and so can discuss the feasibility and wisdom of making synthetic food. Every component except B_{12} can now be manufactured; no doubt even that strange molecule will be synthesized soon. Two questions now arise: first, which nutrients are more economical to synthesize rather than to grow? And second, would the synthetic product be available to people in all parts of the world where it is needed? Pyke uses "synthesis", with commendable strictness, to mean production by purely chemical processes (though the parent substance may be a product of agriculture such as glucose); he does not therefore include conversions brought about by fermentation. In principle, the starting products could have been CO_2, NH_3 and so on. In essence, Pyke agrees with the remark attributed to Steinmetz, in conversation with Baeyer: "You can make indigo more cheaply than God, you will probably be able to make rubber more cheaply than God, but you won't make starch or cellulose more cheaply than God". Few other limitations on synthesis are foreseen.

Cheapness depends on the scale of production and the amount of effort put into improving the processes used. The effort expended depends partly on the natural impulse of an expert to be as efficient as possible; it is also stimulated by competition. A scientifically based industry is likely to be so superior to peasant farming and processing techniques that the peasant industry disappears. There is then little incentive to start the agronomic and biochemical work that would be needed to give the "natural" product any hope of being competitive. But it is legitimate to wonder whether, in every instance where synthesis has prevailed, the "natural" product would not have been cheaper had a comparable amount of research been done on it—especially research aimed at producing multipurpose plants.

When food is being handled by mass production methods and is being distributed through supermarkets, synthesis is probably the cheapest way of obtaining many of the factors that can advantageously be added to it; there is no reasonable alternative to synthetic vitamin A or C in packaged foods. Similarly, the nutritional value of many of the protein sources destined for inclusion in "broiler" rations is greatly enhanced by adding small amounts of methionine. Pyke is so carried away by these facts that he tends to overlook the fact that the people most in need of help do not eat packaged foods and could not use "broiler" methods of animal feeding. The first paragraph of his book asserts that the "complex life of a modern community" would be just as impossible without adequate housing, paper, clothing and transport as without adequate food. That may be true; but it is possible to be less complex. He glosses over the fact that peoples' food requirements are similar wherever and however they live; the amount of clothing and paper that they use varies dramatically. This parochial outlook leads him to disparage various projects for local production of better foods from local products by simple means. Overlooking his own usefully reiterated figures showing the steady diminution in the costs of making amino-acids and vitamins, he says these novel foods are too expensive. How can one tell until they have been made in bulk? The important point is that local methods do not depend on the continuing goodwill of outsiders.

To round off this survey of the place of synthetics in supermarket nutrition, there is a chapter on "non foods"—edible rubbish guaranteed to do the consumer no good. The long term consequences of a community with its guts stuffed with alginates, methylcellulose and plastics are not discussed—but bacteria have interesting adaptive abilities!

N. W. PIRIE

The Arctic at Risk

Productivity and Conservation in Northern Circumpolar Lands. By W. A. Fuller and P. G. Kevan. (Proceedings of a Conference held at Edmonton, Alberta, 15–17 October 1969. IUCN Publications, New Series No. 16.) Pp. 344. (International Union for Conservation of Nature and National Resources: Morges, Switzerland, 1970.)

THIS symposium of thirty-six short papers covers a very wide range of subjects, chiefly concerned with ecological problems of conservation in terrestrial regions of the arctic and subarctic, and to a lesser extent with measurements of the primary and secondary productivity of the principal ecosystems. It brings together reports from work going on in Alaska, the Canadian arctic, Greenland, and the arctic parts of Europe and Siberia.

The first contributions include a brief but masterly review of the essential features of the climate of the tundra zone, illustrated by a series of maps, and a review of the complex interrelations between permafrost and vegetation. This is followed by several papers devoted to the general characteristics of vegetation with a special emphasis on primary productivity and the limitation imposed by the very short growing season, low irradiance and low rates of nutrient turnover. Research on mammals is summarized in papers on reindeer, lynx, polar bear and arctic fox. Finally, the problems of conservation are reviewed in terms of wild life management, utilization of mineral resources and human population.

The symposium as a whole carries a clearly defined and urgent warning which is well supported by the evidence presented. Vegetation and animal populations in arctic lands are beautifully adapted as a delicately balanced whole to a very harsh environment. Exploitation of the animal populations by hunting, though sometimes regrettable in its insensitivity to their decline, has not caused losses that could not be reversed through international cooperation. But the exploitation of the mineral resources of the arctic and development of land communications causes damage of a different order of magnitude. Heavy vehicles, by destroying vegetation and compacting the humus, so alter the thermal conductivity of the ground that the heat balance is changed and melting of the permafrost is initiated. A single passage of a vehicle can start a process of irreversible thermal erosion, leading in a few years to the formation of gullies many feet in depth. The disposal of waste presents a special problem when all decomposition is prevented by low temperatures, and there are no bushes to cover up the heaps of discarded oil drums and other refuse. Bad habits which may pass in the temperate regions become intolerable in the arctic.

It seems proved beyond reasonable doubt that the land surfaces of the arctic are extremely vulnerable to many normal activities of modern man. The vegetation and animal life are at the limit of their tolerance and their survival depends on their precise adjustment to small scale features of the environment. A very slight change in this environment usually has quite disproportionate effects and may result in devastation. The exploitation of the arctic regions requires a thorough scientific analysis of these problems, if irreversible damage is not to become widespread.

C. D. PIGOTT

Wright Preserved

An Original Theory or New Hypothesis of the Universe, 1750. By Thomas Wright. A Facsimile Reprint together with the first publication of "A Theory of the Universe, 1734". Introduction and Transcription by Michael A. Hoskin. (History of Science Library: Primary Sources.) Pp. xxxvii + 178 + 31 plates. (Macdonald: London; Elsevier: New York, February 1971.) £10.00.

THIS addition to the Elsevier History of Science Library is primarily a facsimile of Thomas Wright's *An Original Theory of the Universe,* which was published in 1750 and which made Wright famous as the first person to appreciate the true nature of the Milky Way; an effect resulting from the immersion of the solar system in a much greater star system. Generally, Wright is perhaps credited with rather more than his due measure of respect in this context, for he did not conceive the idea of our galaxy as a disk of stars, but rather preferred to explain the observations in terms of a "galaxy" made up of spherical shells of stars. This does not, however, detract from the historical importance of his work.

But if he has received more than his share of the credit for discovering the nature of our galaxy, Wright's more far reaching theories of the universe have tended to be overlooked, his name being firmly established on the basis of one great discovery, rather than receiving the more general acknowledgment which his widely ranging ideas merit. Notably, his speculation that "the endless Immensity is an unlimited Plenum of Creations not unlike the known Universe" comes close to the realization that the universe (in the modern sense) is populated by galaxies of which our own is an unremarkable individual example. Although the mystic and religious associations brought into his work prevented Wright from making this final theoretical step, his work is well worth the wide attention which this reproduction should bring to it.

Dr Michael Hoskin's excellent introduction adds considerably to the merit of the volume as a whole, setting the theory of Wright in its historical perspective, and providing a very complete account of how the ideas developed from their first primitive form. In this context, it is fascinating to read the first ever publication of Wright's "A Theory of the Universe", written in 1734, when the author was only 22 and had received little formal education in the subject in which his ideas became so prominent. There can be few scientific works which have waited for over two hundred years for publication; as late as 1898 this manuscript was purchased, together with the bulk of Wright's papers, by Newcastle Central Library for only £3.00. A bargain then, the belated publication of the work provides an added bonus now for purchasers of this volume.

Apart from its importance to the history of astronomy, this facsimile is a very high quality reproduction of the original, the proliferation of plates being remarkable for an eighteenth century work. As the beautiful original is now exceedingly rare, bibliophiles will certainly welcome this copy. Astronomers may be more interested in the opinion that "could we view Saturn thro' a Telescope capable of it, we should find his Rings no other than an infinite Number of lesser Planets, inferior to those we call his Satellites", while, having been shown in "Letter the Fourth" that the Sun lies at the centre of a family of planets and comets, they may well be prepared to answer the question of the likely content of space near other stars in the way Wright proposes—"Your Answer, I think I may venture to say, would not be nothing; and methinks I already hear you say, Why Planets such as ours."

JOHN GRIBBIN

For Want of Iron

Iron Deficiency: Pathogenesis, Clinical Aspects, Therapy. By L. Hallberg, H. G. Harwerth and A. Vannotti. Pp. xi + 628 + 16. (Academic: London and New York, December 1970.) £6.00; $18.50.

IN 1963, a Ciba Symposium on "Iron Metabolism" was held in Aix-en-Provence, and in due course the proceedings were published (*Iron Metabolism,* Springer-Verlag, Berlin, 1964). The fifty-eight participants gave an up to date account of the basic and clinical aspects of the subject. This newer publication is an account of the papers given at a similar symposium organized by Geigy in Arosa, Switzerland, in 1969. On this occasion there were seventy-six experts taking part, twelve of whom had attended the earlier meeting. In each instance, the discussion following the papers is published, and it is of considerable interest to see the extent of progress during six years. Fortunately, each book contains an index. All the papers in *Iron Deficiency* are in English. There are three sections which deal respectively with the "Pathogenesis", "Clinical Aspects" and "Therapy of Iron Deficiency", and the following 38 pages are taken up with an account of a panel discussion on "Iron Therapy in Clinical Practice".

This is an essential book for anyone working in this field of interest, the amount of knowledge that is contained in it being very considerable. As might be expected, all aspects of iron metabolism are dealt with in detail, including iron stores, biochemical functions, regulation of iron transport, factors affecting absorption, and the supply and utilization of food iron, together with requirements during growth and pregnancy, and menstrual and other losses. The discussions are of considerable interest, highlighting, as they do, current gaps in knowledge. This more basic material occupies about 400 pages. The clinical section includes accounts of the prevalence of anaemia in certain European countries, but the chief value of the publication lies in the earlier part of the book. The size, comprehensiveness and value of the chapters vary tremendously: the largest contribution, by H. C. Heinrich of Hamburg, deals with intestinal absorption of iron in man and extends through 80 very detailed pages of information. The smallest contribution, by Dresch of Paris, deals with the prevalence of iron deficiency in France and contains about 350 words.

One aspect of the subject, about which various workers are not in agreement, concerns the factors that affect iron absorption, and particularly the importance or otherwise of gastroferrin. This is referred to and discussed by various workers.

In summing up the views expressed at this excellent symposium, Carl Moore makes the important point that, unlike man, many experimental animals absorb ferric and ferrous iron equally well. He refers, too, to the degree of sophistication of ferrokinetic studies and how studies of iron absorption have been facilitated by the development of whole body counters. RONALD GIRDWOOD

Nematodes in Action

The Behaviour of Nematodes: Their Activity, Senses and Responses. By Neil A. Croll. Pp. ix+117. (Arnold: London, November 1970.) £2.25.

THE author has collected the scattered information about the behaviour of animal, plant and free living nematodes and presented it as a review for research workers and students. The book is mostly about movement and the responses of nematodes to external stimuli; descriptions of many behaviour patterns such as feeding are omitted. Nematode responses are discussed in individual sections each devoted to a stimulus type, light, temperature, chemical, electric, gravitational and mechanical. Other sections describe movement activity, aggregation and orientation. Most relevant papers seem to be included in the bibliography, and the book is a useful source of references for further study. There are indices to both subjects and species.

The style is pleasant and the text readable although occasionally verbose and vague, or so brief that an idea is not fully defined and statements appear contradictory. A few words are misused and some jargon introduced but less than in many scientific publications. Often Croll has been shy about using his experience to guide readers so that after reading his summary of published work we have to draw our own conclusions and decide where further research is needed. He has, however, introduced new ideas into some sections deriving information from work on animals other than nematodes.

The index is adequate but has several pagination errors and omissions. Some indication of the pages where a subject is discussed in detail would help the reader, but printing and proof reading errors are few. C. D. GREEN

Molecular Spectroscopy

Physical Chemistry: An Advanced Treatise. Vol. 4: Molecular Properties. Edited by Henry Eyring, Douglas Henderson and Wilhelm Jost. Pp. xix+832. (Academic: New York and London, September 1970.) £18.20.

THIS volume contains fourteen chapters written by a number of authors. There is an introduction by S. H. Bauer to the various topics covered, which include molecular rotation by C. C. Costain, vibrations of molecules by G. W. King and vibrational spectra by J. R. Hall. Radical spectra are covered by D. E. Milligan and H. E. Jacox, and T. Shimanouchi writes on molecular force fields. The interactions between electronic, vibrational and rotational motions, and the electric moments of molecules are considered by J. T. Hougen and A. D. Buckingham respectively. There are accounts of nuclear magnetic resonance (R. M. Golding), electron spin resonance (H. G. Hecht), nuclear quadrupole resonance (E. Schempp and P. J. Bray), Mössbauer spectroscopy (N. N. Greenwood), molecular beam spectroscopy (C. R. Mueller) and, finally, electron diffraction in gases (S. H. Bauer).

The volume is well edited, the nomenclature and symbolism being consistent throughout, but it is disappointing that SI units and equations appear only (as alternatives to c.g.s. units) in Buckingham's chapter. What is difficult in books of this type is to establish amongst the authors a common view of the level and standard of the articles required. Here the editors have been less successful: articles range from excellent introductions, written with authority, to reviews, some thorough, some not and some which assume so much prior knowledge as to make them useful to research workers in the field only.

Although the articles do not attempt to be encyclopaedic, they should summarize the state of development of each topic. The n.m.r. chapter, which makes the subject seem unduly complex, fails to deal with solid state studies and considers but perfunctorily studies of partially orientated molecules (it also gives the symbol "J" a novel meaning). The e.s.r. chapter takes no account either of gaseous species or of neutral radicals in solution; optical methods only are discussed in the study of the spectra of radicals: and no experimental evidence is given for the breakdown of the Born–Oppenheimer approximation, although the theory of the effects is discussed with insight. The chapter on molecular beam spectroscopy lacks detail. I recommend the chapters by Costain, Buckingham, Shimanouchi, Schempp and Bray and Greenwood; the chapter by King includes a very clear introduction to Group Theory.

At a third of the price, this volume could be on every undergraduate's bookshelf, alongside a good book on magnetic resonance. As it is, all readers should leave its purchase to the richer libraries. K. A. MCLAUCHLAN

Geochemical Data

Handbook of Geochemistry. Volume II/2. Executive editor: K. H. Wedepohl. Editorial board: C. W. Correns, D. M. Shaw, K. K. Turekian and J. Zemann. Pp. iv+667. (Springer-Verlag: Berlin and New York, 1970.) Loose-leaf binder, 212 DM; $58.30.

MY chief criticism of the first loose-leaf instalment of volume two of the *Handbook of Geochemistry* was that all material for an element had not been collected before publication of that particular chapter. The appearance of part two hardly eases the frustration engendered by this continuing procedure. Only three further chapters (iron, tin and mercury) have been completed to be added to the finished contributions on carbon, scandium, germanium and rhenium. Partial data for twelve new chapters are now published, but there are still twenty-five elements (including nitrogen, silicon, nickel and copper) for which there is yet no information.

On the production side Springer-Verlag will not win friends with this second instalment. First, the price of the new part (slightly under nine cents per page, as against less than five and a half cents for volumes one and two, part one) has risen at a rate that seems excessive, even in these days of cost inflation. Are subsequent instalments to suffer similar price increases of almost sixty per cent over twelve month periods? Second, surely the publishers could have ensured the same positioning for the punch holes of the pages in the two published parts. So poor is the positioning in the separate parts that when the chapters are arranged in their correct element order, there is a five millimetre variation in the registration of the page margins. Furthermore, thirty-eight sheets are punched on the wrong vertical margin so that the chapter "Yttrium and the Lanthanides" has to be read from back to front, unless it is removed from the file.

The scope of the work, its high standard of text and figure presentation, and the extensive literature coverage are still matters for editorial congratulation. Publication of part two on schedule is also commendable.

DUNCAN MURCHISON

Obituary

Dr G. A. Reay

GEORGE ADAM REAY, formerly director of the Torry Research Station, Aberdeen, died on January 20 after a brief illness. He was sixty-nine.

He was one of the small, enthusiastic and outstanding team of British workers which, initially under the leadership of the late Sir William Bate Hardy, pioneered the study of the various aspects of food science and technology. He obtained his MA (1921) and BSc (1923) at Aberdeen University and won a Senior Kilgour Scholarship. In 1924 he was awarded a Studentship of Emmanuel College, Cambridge, and studied aspects of pancreatic activity and carbohydrate metabolism under the late Sir Frederick Gowland Hopkins at the Sir William Dunn Institute. He was awarded a Carnegie Research Fellowship in 1926 and obtained his PhD (Cantab) in 1927.

In September of the same year he joined the Food Investigation Organization of the Department of Scientific and Industrial Research and was posted to Aberdeen to study the possibility of improving methods of handling "white" fish at sea. It was characteristic of the man that he began his investigations at sea on commercial trawlers rather than in the laboratory; this early work threw much needed light on some of the basic factors affecting spoilage and it led to recommendations for good handling practice that have required little modification over the years. When Torry Research Station was opened in 1929, Reay had already gained valuable field and research experience in freezing and cold storage; he was one of the first to stress the importance of low temperature storage to obtain a good product, as well as rapid freezing, a view at variance with contemporary thinking, and he led the work on freezing at sea, which was first applied commercially in the early 1960s.

Dr Reay is survived by his wife, son and daughter.

Academician A. I. Alikhanov

THE death occurred, on December 8, 1970, of Academician Abram Isaakovich Alikhanov, one of the leading physicists of the Soviet Union.

Alikhanov was born in 1904, in Gandzha (now Kirovabad), in Azerbaijan. He was educated at the Leningrad Polytechnic Institute. After his graduation in 1931, he specialized in nuclear physics and cosmic radiation. In 1934–37 he was the first to study the basic laws of positron formation by means of gamma rays, and investigated problems of beta-decay. With his brother, Artemii Isaakovich Alikhanyan, he began a programme of systematic study of the beta-spectra of synthetic radioactive elements. During World War II, he set up a laboratory in Armenia where he developed a new method of studying the composition and energy spectra of cosmic rays.

In 1945, Alikhanov founded the Institute of Theoretical and Experimental Physics, remaining as its director until 1968. There, he and his brother developed a large spectrometer for studying the mass spectra of cosmic ray particles. In 1949 he put into operation the first Soviet reactor with a heavy water inhibitor, and was one of the designers of the first Soviet atomic bomb. In 1961, on his initiative, the Institute of Theoretical and Experimental Physics produced a 7 GeV proton synchrotron, and he later took a leading part in the development of the Serpukhov 70 GeV proton accelerator.

He was elected to the Academy of Sciences of the Soviet Union and the Armenian Academy of Sciences in 1943, and became Chairman of the Commission for the Study of Cosmic Rays of the Academy of Sciences of the USSR in 1959. His publications include *Investigation of Artificial Radioactivity* (1936), *New Data on the Nature of Cosmic Radiation* (1945), *Cosmic Radiation* (1949), *Weak Interactions* (1960) and *Experiment* (1962). He was awarded the Order of Lenin three times, a State Prize for physics and a number of medals.

Announcements

University News

The Council of the **University of Birmingham** has approved the appointment of a review body "to consider the role, constitution and functioning of the University of Birmingham and to make recommendations to Council for any desirable changes". The review body would now welcome written submissions of evidence from any person or organization concerning any part of the matter within its terms of reference. Written evidence should be sent to the secretary, Sir Maurice Dean, Winterbourne, 58 Edgbaston Park Road, Birmingham B15 2RT, not later than March 31. Persons or representatives of organizations may later be invited to appear before the review body.

Appointments

Professor Henry Charnock, University of Southampton, has been appointed director of the **National Institute of Oceanography** in succession to **Sir George Deacon**.

Miscellaneous

The **Zoological Society of London** has made the following awards for 1970: *the Stamford Raffles award*, to **Mr D. R. Rosevear**, an amateur zoologist, for his contributions to the knowledge of West African mammalian fauna; *the scientific medal*, to **Dr Denis Noble**, University of Oxford, for his work on the physiology of nerve and muscle and to **Professor J. G. Phillips**, University of Hull, for his work on comparative zoology; *the Thomas Henry Huxley award*, to **Dr P. J. Sharp**, University of Leeds, for his doctoral thesis "The hypothalamic control of gonadotrophin release in the Japanese quail (*Coturnix coturnix japonica*)"; a certificate will be presented to **Dr O. Anne E. Rosa**, University of London, whose doctoral thesis was highly commended; *the Prince Philip prize*, to **Stephen M. Clift**, Archbishop Holgate's Grammar School, York, for his essay "Some characteristics of the shells of limpets, *Patella vulgata*, in relation to the environment".

ERRATUM. In the article "Menstrual Synchrony and Suppression" by Martha K. McClintock (*Nature*, **229**, 244; 1971), the last sentence of the fourth paragraph should read: "In addition, subjects estimated how many times each week they spent time with males (for example, dating, visiting informally or conversing at length with male professors) and listed by room number the girls ($N \leq 10$) with whom they spent the most time, indicating which two of these they saw most often".

International Meetings

April 5–6, **Flames, Flammability and Fires,** Swansea (Professor D. F. Cullis, Department of Chemistry, The City University, London EC1).

April 6, **New Materials and Trends in the Water Industry,** London (Mr E. S. Hall, 69 Disraeli Crescent, High Wycombe, Buckinghamshire).

April 14–16, **Tissue Growth and Interaction during Development** and **Interactive Behaviour of Cells.** Aberystwyth (Professor Bryn Jones, Department of Zoology, University College of Wales, Aberystwyth, Wales).

May 12, **Environmental Health,** Detroit (Alan J. Hitsky, Information Services, Wayne State University, Detroit, Michigan 48202, USA).

British Diary

Monday, March 1

How to Enjoy Food Additives (6.30 p.m.) Professor B. C. L. Weedon, Society of Chemical Industry, London Section, jointly with the Food Group, at 14 Belgrave Square, London SW1.

Telecommunications—New Practices, Old Concepts (5.30 p.m.) Professor J. Greig, Institution of Electrical Engineers, at Savoy Place, London WC2.

The Use of Computers in Aircraft (7 p.m.) Mr B. J. Calvert, Institution of Electrical Engineers, at the Royal Star Hotel, Maidstone, Kent.

Tuesday, March 2

Adaptation in Mammals (5.30 p.m.) Professor R. J. Harrison, Royal Institution, at 21 Albemarle Street, London W1. (Lecture for Sixth Form Pupils from Schools in London and the Home Counties. To be repeated on March 3, 9 and 10.)

Environment in Ships (6.30 p.m.) Society of Environmental Engineers, at BAC, Bristol.

Excavations at Swanscombe 1970 (5.45 p.m.) Dr J. d'A. Waechter, University of London, at the Institute of Archaeology, 31–34 Gordon Square, London WC1.

Industrial Innovation (5.30 p.m.) Professor C. Freeman, Institution of Electrical Engineers, at Savoy Place, London WC2.

Technical Codes of Practice in Independent Television (5.30 p.m. discussion) Institution of Electrical Engineers, at Savoy Place, London WC2.

Wednesday, March 3

A British Railway's Development—The Advanced Passenger Train (7.30 p.m.) Dr S. Jones, Institution of Electrical Engineers, at Dorking Halls, Dorking, Surrey.

Colour in Architecture, Mr D. L. Medd; **Studies on Surface Texture by Goniospectrophotometry,** Mr M. P. Wassall (3 p.m.) Colour Group (Great Britain), in the Physics Department, Imperial College, Prince Consort Road, London SW7.

Giovanni Battista Morgagni's "De Sedibus et Causis Morborum per Anatomen Indagatis", Venice, 1761 (1 p.m.) Professor J. Steudel, Royal Institution, History of Science Discussion Group, at 21 Albemarle Street, London W1.

Loran C—Some Recent Developments and Field Observations (6 p.m.) Mr W. F. Blanchard and Mr A. R. Woods, Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

Medical and Veterinary Applications of Clean Air (2.30 p.m. symposium) Society of Environmental Engineers, in the Mechanical Engineering Department, Imperial College, London SW7.

Recent Advances in Microscopical Techniques of Particle Characterization (2.30 p.m.) Society for Analytical Chemistry, Particle Size Analysis Group, in the Link Lecture Theatre, The University, Leicester.

Solid State Control of Electrical Appliances (5.30 p.m. discussion) Institution of Electrical Engineers, at Savoy Place, London WC2.

Thursday, March 4

Art and Science Now : the Possibility of Convergence (1.30 p.m.) Mr P. D. Carpenter, University of London, at Imperial College, London SW7.

Have Physicists Lost Their Imagination? (1.20 p.m.) Professor D. H. White, University of London, in the Botany Theatre, University College London, Gower Street, London WC1.

Mechanical Behaviour of Polymers under Low Temperature High Frequency Cycling (6.30 p.m.) Mr J. L. Prosser, Oil and Colour Chemists' Association, at the Royal Turks Head Hotel, Grey Street, Newcastle upon Tyne.

Recent Developments in Ergot Research (5.30 p.m.) Dr Albert Hofmann, University of London, at the School of Pharmacy, 29–39 Brunswick Square, London WC1.

Reflection, Refraction and Polarization of Light. Refraction and Scattering of Light (1 p.m. films) Royal Institution, at 21 Albemarle Street, London W1.

Solvent-free Coatings (7 p.m.) Dr F. Blomryer, Oil and Colour Chemists' Association, at the British Rail School of Transport, London Road, Derby.

The Post Office as a Business (5.30 p.m.) Mr A. W. C. Ryland, Institution of Electrical Engineers, at Savoy Place, London WC2.

The Response of Scientific Advances in the Field of Water Management (6 p.m.) Sir Norman Rowntree, British Hydromechanics Research Association, at the Royal Institution, 21 Albemarle Street, London W1 (Third Fluid Science Lecture).

Friday, March 5

New Frontiers for Research and Development (9 p.m.) Dr H. E. Thiemann, Royal Institution, at 21 Albemarle Street, London W1.

Psychoactive Substances from the Plant Kingdom (5.30 p.m.) Dr Albert Hofmann, University of London, at the School of Pharmacy, 29–39 Brunswick Square, London WC1.

Reactions of Radicals Derived from Carcinogenic Aromatic Amines (1 p.m.) Mr M. J. Carey, Royal Institution, Photochemistry Discussion Group, at 21 Albemarle Street, London W1.

Monday, March 8

Communication of Objectives—Reconciling the Interests of the Organization and the Engineer (5.30 p.m.) Dr D. Pym, Institution of Electrical Engineers, at Savoy Place, London WC2.

"Ford Commuter" — Electric Urban Vehicle (6.30 p.m.) Mr T. K. L. Dobedoe and Mr R. F. Robbins, Institution of Electrical Engineers, London Graduate and Student Section, at Thames Polytechnic, Wellington Street, London SE18.

Recent Progress on Semiconductor Microwave Sources (2 p.m. colloquium) Institution of Electrical Engineers, at Savoy Place, London WC2.

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Computers, Conservatives and Governments

Sir John Eden seems to have done a great deal to make the British Government's attitude towards industry at large applicable to the British computer industry (see page 4), for it is only reasonable that a government which could let Rolls-Royce go bankrupt should take away from the largest computer manufacturer the sense of sponsored security which it has enjoyed since its formation. The principle on which the government appears to be working is that expressed somewhat over-directly by Mr John Davies, the Minister for Trade and Industry, some months ago, that industry should no longer expect the government to bail it out. What Mr Davies and his colleagues intend is that industrial organizations of all kinds should be much more aware than in the past that the penalty of failure is not humiliation or even a government subsidy but the actual disappearance of a commercial organization, factories, jobs and even boards of directors.

Up to a point, it will be valuable for everybody in Britain (as well as for customers of British companies abroad) if the sense of urgency which the government is seeking to impart to industry does actually lead to a more competitive and more hardnosed view in British companies about the objectives of all commercial enterprises. There are, however, several pitfalls in a simple application of this doctrine, not the least of which is that the present government could easily be a long way towards a demonstration that the government's word is not to be taken over-seriously. After all, ICL is itself a child of what seemed at the time a shotgun marriage of computer manufacturers organized by the old Industrial Reorganization Corporation. Whether or not the government formally agreed to keep ICL's interests close to its heart, there is very little doubt that the merger would never have come to pass if an impression of security and even subsidy had not been created. In many ways, the case of ICL resembles very closely that of Rolls-Royce Limited, where it is unlikely that a consortium of banks would last year have helped to tide the company over its shortage of cash if there had not been a widespread belief that no government could let that jumped-up motor manufacturer go to the wall. One of the questions which has been raised by the Rolls-Royce decision and that on ICL is, in short, whether industrial companies can allow themselves to rely for long-term planning on the implicit promises of governments which must necessarily be comparatively short-lived. Another way of putting the same question is to ask whether governments should not somehow be constrained in their relationships with industrial companies by the need to be committed by their predecessors' implicit promises. That is a serious question which needs more careful discussion than it has received so far.

For the rest, the new government's decision that in future ICL should stand on its own feet raises important questions about the management of such a company based in Britain but seeking somehow to compete with the world at large. The problem is different from that which faced Rolls-Royce, for there is no question of being committed to an over-grandiose project that dwarfs the rest of the company's business. By the same test, ICL is not in the position of the aircraft manufacturers busy in the development of the Concorde aircraft, by now persuaded that their commercial success depends entirely on the success of the machine they are trying to construct but uneasily aware that it is becoming the tail that wags the dog. What ICL is trying to do is to be all things to all customers—a supplier of very small special purpose computers and very large general purpose machines. Its handicap is that its reputation in the field is not nearly strong enough for it to be able to sell successfully without trimming its prices to get the business, which means that a disproportionately small part of its resources can be spared for the kind of research and development on which the company's success must in the long run depend. The trouble, alas, is that no amount of native wit nor even of ingenuity can be certain to overcome this fierce obstacle. As always since the previous government set about creating the general purpose computer company, there is now a danger that ICL will be squeezed between the very large international manufacturers such as IBM and the comparatively very small companies which specialize in the manufacture of computers for particular purposes. Its continued existence is in short a reminder of the inconsistencies or at least the imperfections of the Labour Government's doctrine that size means strength.

The most obvious difficulty is that diversity is itself a weakness if not supported by sufficiently diverse research and development. This is one sense in which high technology differs from low technology. For ICL, the strategy now should be to attempt to concentrate its resources on some field in which it can hope to make a sure footing for itself. On the face of things, the most likely place in which to dig in the heels will be the design and manufacture of very large computers, for here at least is a set of circumstances in which the government is certain in the next few years to be such a ready customer that no amount of self-denial can put ICL entirely out of court. For the government, the moral of the situation which has now arisen is that it must somehow in the next few years create a climate in which comparatively small computer manufacturers can make a way for themselves in a competitive world by offering other kinds of special services. All kinds of possibilities suggest themselves. It is hard, for example, to believe that it must indefinitely be necessary to rely on general purpose machines for such functions as the control of automatic machine tools or typesetting equipment. And what of the chances that specialized kinds of computers will in due course be devised for satisfying the needs of particular kinds of customers? And is there not a case for thinking that the computer manufacturer who first manages to market his machinery in such a way as to satisfy not merely the ego but the need of his customer will have a powerful competitive edge? The modern world, after all, is almost as full of disappointed computer owners as of computers.

But how can an ostentatiously *laissez faire* government hope to influence the direction of technical development? This is a question for Mr Davies as well as for the Chancellor of the Exchequer, Mr Anthony Barber. It has in the past few months been too easily assumed that there is nothing that can be done without compromising principles. After all, even the Conservative government has kept in being the very large apparatus for the conduct of research and development in the civil fields. Even after months of declarations that people must now stand on their own feet, all kinds of research laboratories that might have been abolished find themselves still in existence. Would it not make sense to ask that some of these should more obviously than in the past lend their energy to the development or at least the support of new technical developments in computers? Indeed, there are the strongest of reasons for asking that the government should devise some way of using the apparatus of public research and development for encouraging technical development of a kind that seems to be desirable. In the United States, where public laboratories are far thinner on the ground, the Federal government undertakes the corresponding responsibility of letting research and development contracts with industrial companies. One of the paradoxes of the new Conservative government's philosophy is that it has kept much of the apparatus of public intervention in industry which the Labour government set up or inherited, but has resolutely decided not to use it, and has at the same time foresworn the devices by means of which other kinds of governments seek to use industry for the creation of national prosperity. In short, the new Conservative government is a little like a boxer who decides not to use one fist and who ties the other behind his back.

How will the Universities be Nourished?

THESE are bad times for British universities, as any academic can tell by reading between the lines of the latest report from the University Grants Committee (see page 5). What most of all afflicts the committee is the uncertainty about the future which has been occasioned partly by the way in which the Department of Education and Science has been muttering at the high cost of present arrangements, partly because of the difficulty of predicting what students will ask of the university system, partly because of uncertainty about the relationships between the universities and other sectors in the British system of higher education such as the polytechnics and partly because, in any case, the committee is already deeply immersed in planning for the next quinquennium, due to start in September 1972, and because it is, as always, uncertain of the outcome. In circumstances like these, it is perhaps too much to ask that academic planning should be a tranquil business, yet there is enough evidence in the recent trend of events to show that some at least of the present uncertainty could be removed.

Where the government is concerned, the most urgent need is for a declaration of policy. To say, as the government does, that higher education is a good thing and that there should be more of it begs questions such as the extent to which institutions of all kinds, from colleges of education to universities, can rely on finding money in the years ahead. In the past few years, the universities have been compelled by successive waves of economy and increases of costs to regard themselves as comparatively poor relations of the polytechnics, until now almost universally the apples of the local council's eyes. But nobody can be sure that current pressure on local authority finance will enable the polytechnics to continue living as freely as they have in the recent past. Indeed, there is a danger that when the local authorities turn mean, they will be able to do so individually and privately, thus turning prosperity into penury without the outside world knowing what is afoot. Then, to be sure, it may be much easier than at present for the polytechnics to swallow their recent pride and make common cause with the universities. The danger is that by that time, the universities themselves will be so overwhelmed with immediate problems that they will be unable to take part in the marriage which they now profess they seek. In circumstances like these, the issues of how to find a uniform framework within which to finance all parts of the higher educational system, the colleges of education as well as the polytechnics and the universities, and a common system for selecting students, should not be ignored simply because they are uncomfortable.

For the universities, there is an urgent need for better arrangements for coordinating academic enterprises. In the past few years, the University Grants Committee has not been nearly as successful as it might have been in bringing about a more rational pattern of teaching. Although it is clear that there are far more universities per square mile in Britain than are necessary to enable students to sit at the feet of some teacher or other, the universities have been uncommonly slow to arrive at a sensible division of labour among themselves. If one university sets up a chair of applied Sanskrit, for example, there is still a danger that others nearby will try to follow suit.

The University Grants Committee has in the past made a few efforts to rationalize the pattern of teaching in, for example, agriculture, but has in the process burnt its fingers so badly that it has fought shy of other ventures. Yet there are good reasons to expect that rearrangements of this kind could bring great economies and, by extension, greater freedom. As things are, it seems to have been left to the research councils to create a tendency towards specialization among the universities. In the long run, no doubt, the result will be as beneficent as the largely enlightened management of the research councils can make it, but this unfortunately is only half a reassurance. It would be better and safer if the universities as such were more directly in charge of their own destiny. Everybody will acknowledge that present uncertainties about government policy must make the University Grants Committee unsure of itself, but there is no excuse for not carrying out good housekeeping while waiting to see which way the wind will blow.

Who will Referee the Referees?

ONE of the most contentious issues in modern science is the institution of the referee—the system by means of which anonymous, devoted and skilled professionals spend their energy on the evaluation of scientific articles submitted for publication. Journals such as *Nature* would not flourish without the referee. But if in some quarters referees are highly respected, elsewhere they are often reviled. Disappointed authors fight long wordy battles with their unknown critics and, for every man who says that he has valued what the referee has had to say, there is at least one other who bristles fiercely at what he supposes to be an attack on his professional integrity. In circumstances like these, anything that throws light on the way in which the referee system functions is likely to be valuable. An article by Dr Harriet Zuckerman and Professor Robert K. Merton in the current issue of *Minerva* (**9**, 66; 1971) is to be welcomed even though in many ways the document misses the chief question to be decided—what are referees for?

Much of what Zuckerman and Merton have to say is based on a study of the complex of journals published by the American Institute of Physics and especially *Physical Review*, the house journal of the American Physical Society. One of the merits of the article, however, is the reminder which it provides that—contrary to expectation—scientific journals are less choosy about the articles they publish than journals in history, philosophy and the like. Although there is no doubt fierce competition for space in journals such as *Physical Review Letters*, the top of the pecking order of rejection rates among learned journals seems to be occupied by those that specialize in history: of three journals examined in 1967, the average rejection rate is 90 per cent. By comparison, even physics comes a long way down, where twelve journals were discovered to have a rejection rate of 24 per cent. One of the weaknesses of the argument which Zuckerman and Merton put forward shines out—if that is the phrase—from their discussion of this phenomenon. Is a journal which publishes only a tiny proportion of the manuscripts it receives to be praised for the toughness of its editorial policy or despised for rendering such a poor service to its contributors? The trap in all this is to suppose that there is some necessary correlation between an editorial decision to publish an article and the quality of what is published. The truth is, or should be, that journals should have a character of their own which is at least recognizable to those in charge. Just as a journal for the popularization of science will sometimes decline to publish articles which are too didactic or too conceptually difficult for its purposes, and as a daily newspaper will decline to publish articles which have very little to do with current events, so scientific journals with a place to keep will decline to publish articles that do not suit them. To say that a decision not to publish is necessarily a comment on the quality or the integrity of a putative article is to make too much of a simple and valuable property of all kinds of publications—that they must seek to be not so much arbiters of the competence of their contributors as servants of the interests of their readers.

What Zuckerman and Merton have to add to this discussion is an intriguing analysis of the relative status of those who referee and those who are refereed upon. Their sample consists of those contributors to *Physical Review* submitting manuscripts between 1948 and 1956—close on 10,000 altogether. By hunting through the reference books, Zuckerman and Merton have been able to establish the pecking order within this class of physicists—Nobel prizewinners at the top and humble authors at the bottom. Using the same criteria, referees are also divided into categories at different places in the pecking order. Every disappointed author's prejudices will be confirmed by the discovery that the manuscripts of higher ranking authors are dealt with more quickly than those of physicists at the bottom of the pecking order—in the period studied by Zuckerman and Merton, 42 per cent of those manuscripts in the top drawer were dealt with in less than two months but only 29 per cent of what are called third-rank physicists enjoyed this speed. By the same test, referees appear to have been more tolerant of the manuscripts submitted by higher ranking physicists than of those coming lower down, although there is at least one sign of grace, that there seems to be no correlation between the age of an author and the acceptability of his manuscript or between the rank of a referee and the nature of his decision. The question which neither Zuckerman and Merton nor their readers will be able to answer is whether referees can ever be the Solomons authors, referees and sometimes even editors suppose that they must be.

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100 Years Ago

The Duke of Edinburgh in Ceylon: a book of Elephant and Elk Sport. By John Capper, *Times* correspondent. Illustrated with chromo-lithographs. (London: Provost & Co., 1871.)

THIS book is sufficiently described by its title, being a record of the visit of the Duke of Edinburgh to Ceylon last year, and of his success in the colonial sports of elephant hunting and elk hunting. It appeals to two sections of the public, those who eagerly seize upon every incident connected with the mode of life of any member of our Royal family, and those who are equally eager after any description from life of sport in those countries where wild beasts worthy of a hunter's rifle abound. We may quote the following as an instance of the perils encountered by our Prince in navigating the Cingalese rivers. "The stream was teeming with life. Fish of all varieties and sizes sprang into the boats as they paddled along, one of them finding its way into the Prince's coat pocket" (loyal fish !) ; "on all sides could be heard the snapping of alligators' jaws as tiny fish were caught in the monsters' mouths. The party had proceeded about a mile down the stream, when one of them, leaning down and resting his head on the gunwale of the boat, was startled from his quiet rest by the apparition of an alligator's gaping jaws, which made a direct snap at his head, fortunately missing it, but seizing, in place of it, the barrel of the rifle held in the hands of the Prince's English attendant, who was seated next to him, and which the monster nearly wrenched out of his hand, splashing the water about, and drenching every one in the canoe." Is the *Times* correspondent quite certain that alligators are found in Ceylon?

From Nature, 3, 366, *March* 9, 1871.

OLD WORLD

Select Committee Computes ICL's Future

WHAT would be the consequences if International Computers Limited were to follow Rolls-Royce down the slippery slope? That gloomy prospect was the thrust of much of the questioning at last week's meeting of the computer subcommittee of the Select Committee on Science and Technology in the House of Commons. Giving evidence was Sir John Eden, the minister at the Department of Trade and Industry in whose ambit lie the affairs of the computer industry. Sir John obviously thought the questions to be out of turn. ICL, he said, is perfectly capable of standing on its own feet. Following the merger in 1968 when ICL was formed out of ICT, English Electric Computers, and the computing interests of Plessey, the company has built up a strong management team and a clear idea of the market. The British computer industry is in no need of propping up.

In this rosy light, Sir John revealed two new aspects of the government's policy toward the industry. Both affect ICL, but in Sir John's view in neither case significantly. First, the practice of loading the selection procedure for government computers in favour of ICL will end. This measure should close up some old wounds, chiefly among the United States companies which have factories in Britain. Honeywell and IBM claim to be good guests, contributing favourably to the balance of payments, but are discriminated against in orders from the British government.

Second—but probably less important in practice—the government seems now to consider that in exceptional circumstances it would feel free to buy its very large computers from companies other than ICL

Adding these two principles to the news a fortnight ago that the government intends to rely less on its own resources to write its own computer programs (see *Nature*, **229**, 588; 1971), a picture of the attitude of the Conservative government to the industry is now rapidly emerging. All aspects of the new policy have so far been broadcast through the subcommittee, which must be gratifying to its chairman, Mr Airey Neave. Since the computer investigation got under way more than a year ago, the subcommittee has earned a reputation for directing searchlights into awkward crannies, just as its twin subcommittee on space research is at present exposing the absence of thought behind British space policy.

So far, however, the Conservative government has not followed up the reorganization of the old Ministry of Technology with a revision of the obscurities which confuse the government's arrangements for dealing with the computer industry. One of the successes of the subcommittee last year was to point out the deficiencies of a system involving the Ministry of Technology, the Civil Service Department, the Treasury, the Stationery Office, a group called the Technical Support Unit shared between the Ministry of Technology and the Civil Service Department, and a network of interministerial committees. When a government department decides that it needs a computer, the requirement is first discussed between the particular department and the Civil Service Department. The role of the Ministry of Technology was to draw attention to the computers available from firms manufacturing in Britain, and the Treasury is involved to make sure that the user department gets value for money. Finally, the order is placed through the Stationery Office.

Briefly, the role of the Ministry of Technology was to stimulate the use of computers, encourage computer firms to set up factories in Britain, and generally to sponsor the industry. The only change since these functions were taken over by the Department of Trade and Industry, so far discerned by the subcommittee, is that individual government departments are becoming more competent at handling their own computer projects (according to the most recent evidence from the Civil Service Department). The Civil Service Department is therefore retiring from the scene where it can, to search for a more strategic role in planning, the proposal of common policies, and the promotion of technical developments.

Sir John Eden.

But although nobody has poured weed-killer on what Mr Neave used to call the data-processing jungle, attitudes towards the computer industry have changed. Software firms have often asked that Whitehall emulate the United States government which carries out hardly any software work internally. Even defence software, where it might be thought that secrecy would be a problem, has been contracted out. Part of the justification for the new policy, which will result in an increase in the volume of business placed with software houses from £570,000 in 1969/70 to possibly more than £1.5 million in 1971/72, is the high rate of turnover in government data-processing staff, although recent figures show a slight improvement. For example, 11.8 per cent of the number of experimental officers in data-processing at April 1968 had left a year later, but in the twelve months of 1969/70 resignations were only 9 per cent of the experimental officer staff at April 1969. Whether these figures are any worse than the commercial software firms could show is a moot point.

Perhaps this new policy will lead to a consolidation of British software firms, most of which are tiny by American standards, although this is something that the Industrial Reorganization Corporation failed to achieve in its brief life. More to the immediate point, it is to be hoped that the new approach to software will mean an end to the mentality that, according to evidence given to the subcommittee last year, allowed twenty-three payroll systems for use on ICL 1900 machines in government departments to be developed separately.

At least one idiocy has been done away with by Sir John Eden's new policy—the riddle when is a British computer not a British computer will no longer have to be answered. In the past, when competitive orders were sought from several firms, the contract has been awarded on merit but with a preference for the British machine so long as it was not unduly expensive compared with the others. What the price differential can rise to has never been officially stated. But the managing director of IBM (UK), Mr Edwin Nixon, caused a furore last year when he claimed that non-British companies have to tender 25 per cent lower than ICL to get government orders. The situation is undoubtedly more complicated than that. But apart from the ill feeling caused by a policy that has never been fully defined in public, the system has run into problems with computers manufactured in Britain with a significant proportion of British-made components, but by a non-British company (notably IBM and Honeywell which both have factories in Britain). The Department of Trade and Industry has already admitted to the subcommittee that it is sometimes necessary to examine each of a firm's models individually and in detail to decide to what extent it can be called British.

What has the change of government meant for ICL? Sir John Eden affirms that the Conservative government attaches great importance to the existence of a strong, competent, British-owned computer industry. Britain must continue to be able to make a full range of computers. The new policies will not adversely affect ICL, Sir John claims, now that the British computer industry is capable of meeting and beating competition on its own terms. In any case, he points out, the government sector takes less than 10 per cent of ICL's sales. The chairman of ICL, Sir John Wall, is reported as commenting that ICL has never won a contract through the price preference arrangement. In that case little has been gained by the old policy, at the cost of a deal of discontent.

In the opinion of Sir John Eden, the mode of help for ICL in future will be the government's procurement policy, coupled with an intensification of the use of computers in the public sector. With only £38.8 million worth of computers in operation in government departments at the end of last year, there seems to be room for growth. And the government will continue to encourage buyers in the public sector to favour British machines.

All the same, members of the subcommittee were far from convinced by the optimism. The government has already made clear that there will be no more payments to ICL after the final £2.25 million due under the merger agreement is paid this year. And the withdrawal of investment grants which have been particularly favourable to the computer industry is causing concern among the committee. Would the government step in if there was an acute cash shortage in the industry, members of the subcommittee wanted to know? Sir John was uneasy about the question. It is the policy of the Conservative government to encourage industry to rely on its own sources of finance without going to public sources, so it was unlikely that the government would go beyond the role of purchaser of computers. But faced with a hypothetical question, nothing could be ruled out.

The subcommittee was pleased that Sir John was sympathetic to the notion of development grants, however, particularly in regard to Project 52. This is the code-name for ICL work on a new large machine, still under wraps. But the subcommittee was clearly worried about the future of Project 52 now that ICL has joined with the American Control Data Corporation (CDC) and the French Compagnie Internationale pour l'Informatique (CII) to form an organization called Multinational Data that will integrate the range of hardware offered by the three companies. Control Data dominates the market for the largest computers, an area in which even IBM has never succeeded in entering convincingly; does the arrangement mean that ICL will be constrained to specialize in medium-sized machines? Sir John did not think so.

If advantage is taken of the link with CDC, however, it could be ICL's salvation for the next decade, by providing a foot in the door of the American market. Perhaps it will also solve the problem of the British inability to match the American R&D expenditure on computers. So far the subcommittee has not been able to discover precisely how much is spent annually under this heading in Britain. Roughly speaking, it seems that the British computer industry might be spending about £20–£25 million a year, and the government (through the Department of Trade and Industry) about £16–£17 million. But it was astonishing that the representatives of the Department of Trade and Industry who have appeared so far have not been able to put their fingers on precisely how much the government is spending and under what headings. To the subcommittee this must be evidence that not enough attention is being paid to the basic problem—ICL barely has the resources to maintain an R&D programme that will sustain the company in the years ahead. The 360 series is reputed to have cost $3–4 thousand million to develop, and its introduction was traumatic even for a company the size of IBM. How can ICL match that?

UNIVERSITIES

UGC in the Dark

The University Grants Committee has evidently found itself in a cleft stick during the past year. It has had to take decisions about capital expenditure on university buildings up to 1974, but the framework for these decisions has been missing because there has been no indication from the government of the size to which the student population in the universities should grow. Indeed, it seems unlikely that the government will be in a position to make up its mind about the rate of growth in higher education until the middle of 1972, when decisions on recurrent expenditure during the next quinquennium (1972–77) must be announced. The committee in May last year therefore took the law into its own hands, and sent each university a letter indicating the student numbers in 1976–77 that the university might consider as a starting point for its own planning. Mr Kenneth Berrill, chairman of the UGC, outlines in the UGC's annual survey the likely drift of planning in the universities in the light of replies to this letter (*University Grants Committee Annual Survey, 1969–70*, HMSO, 30p).

The shortage of residential accommodation for students is likely to be the chief constraint on expansion unless loan-financed housing schemes can be operated on a more effective basis. The UGC has already been authorized to increase its assistance to loan-financed schemes, and instead of only providing furniture grants, as it has in the past, the committee can now contribute to the overall cost of new buildings. Nevertheless, many universities are uneasy about raising money from private loans, and Mr Berrill says that the whole question needs further study.

Leaving aside limitations imposed by the shortage of residential accommodation, the universities indicated that they could collectively accommodate 285,000 students by 1973–74, 41 per cent of whom would be arts based and 59 per cent science based. But this imposes another constraint on the UGC's planning because it would like to see a mix of 45 per cent arts students and 55 per cent science students—much the same as that which obtains among students at present entering universities. The UGC has therefore found it "necessary to restrict to the minimum the provision of extra accommodation for science subjects, and to give heavy emphasis to the provision of additional capacity in the arts and social sciences".

The UGC's survey also shows that the cost of educating a student at a British university increased from £752.5 a year in 1959–60 to £900 a year in 1966–67. By 1968–69, however, this cost had dropped to £864.3. The staff : student ratio also fluctuated during the 1960s, falling from 8.04 : 1 in 1959–60 to 7.55 : 1 in 1964–65, since when it has been increasing steadily to reach 8.16 : 1 in 1968–69. What will happen to these figures in the next ten years is a moot point, however, because, as the UGC makes clear, "the final target for 1976–77 can be determined only in the light of government decisions on capital and recurrent finance" and this in turn calls for government decisions on the size and structure of higher education.

CANCER THERAPY

Issels' Claims Refuted

Many of the patients whom Dr Issels claims to have treated successfully in his cancer clinic at Ringberg, Bavaria, were cured by radiotherapy or surgery before they were admitted. Confusion about efficacy of the treatment has therefore arisen because severe post-radiation reactions were misdiagnosed as residual cancer and treated as such by Dr Issels. That is the chief conclusion arrived at by a team of British cancer workers who visited the clinic in January at the request of the Joint Co-ordinating Committee on Cancer Research. Reporting on its findings, the team is lavish in its praise of the standards of nursing given to patients in the clinic, but sceptical of the claims advanced by Dr Issels for his treatment (*A Report on the Treatment of Cancer at the Ringberg Clinic, Rottach Egern, Bavaria*, HMSO, 15p). The members of the team say "we are convinced that Dr Issels believes implicitly in the treatment he gives. We think he does a great deal to help most of his patients. We sadly think, however, that he is misguided in his beliefs, and that the treatment peculiar to his clinic is ineffective".

The committee's conclusions are based chiefly on a study of the records of 48 patients treated in the clinic for various types of cancer, and who had survived or were thought to be free from disease between two and twenty-one years later. As far as Dr Issels was concerned, all these patients had terminal cancer when they were admitted to the clinic, but according to the committee, 28 of them showed no evidence of residual tumour—their symptoms were more probably due to over-radiation—six were treated with cytotoxic drugs, two had tumours removed surgically after treatment by Dr Issels and one probably never had cancer.

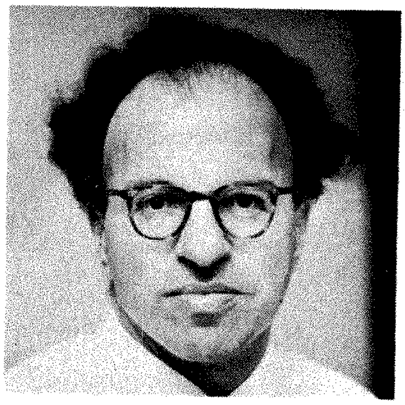
In only eleven patients was there "possibly some evidence of tumour regression" after treatment by Dr Issels' method on its own. But in the committee's opinion, eight of these possibilities rested on such slender evidence that "only by giving the benefit of much doubt could they be included", and the remaining three provide almost the entire evidence that a favourable tumour response results from the clinic's treatment when used alone. Of these three, however, one had no histological confirmation of the diagnosis, one was of low-grade malignancy and the other was benign or at most of marginal malignancy. The committee therefore concludes that "they might perhaps have been accepted in some hospitals as successful results of a treatment method under trial, and we do not believe they would have been so accepted in most; they would not have been so accepted in the hospitals in which we work".

But while the committee pours considerable scepticism on Dr Issels' claims to cure terminal cancer patients, it is no less vociferous in its praise of his nursing care. The strength of Dr Issels' character and the frankness with which he treats his patients often give them renewed hope so that they are "mentally and morally renewed" and severe pain is sometimes relieved without drugs. The committee ends with a gloomy reflexion on the standards of treatment for terminal cancer patients in Britain; "if regular and continued support was always available for the dying, there would be less inclination for patients to seek help abroad. . . . The fact that so many patients go to this clinic to find something they fail to receive at home is really more a reflexion on the medical service they leave than a credit to Dr Issels' particular treatment". It is also a reflexion of the power of the mass media in stirring up public feeling over a sensitive issue such as cancer therapy.

ESRO

New Man at the Helm

A GLIMMER of hope that the European Space Research Organization may be emerging from the doldrums was provided by the election last week of Dr Alexander Hocker to the post of Director-General of the organization. Dr Hocker will take over from Professor Hermann Bondi who became scientific adviser to the Ministry of Defence in Britain on March 1. Professor Bondi himself was known to be sceptical of the possibility that the ESRO council would find a suitable director to take over an organization whose future hangs in the balance. But on February 23, the council had little difficulty in electing Dr Hocker to the post, and he will take up his duties on April 15.



Professor Hermann Bondi.

A former member of the Federal Ministry of Atomic Energy in Germany and of the council of the nuclear research centre at Julich, Dr Hocker played an active role in the formation of ESRO and was chairman of the ESRO council from 1964–67. He is at present a scientific adviser to the board of directors of Volkswagen.

Dr Hocker has a formidable task ahead of him in steering ESRO through its present crisis. At the council meeting last December, the French delegation gave notice that the French government had decided to withdraw from ESRO at the end of 1971. This declaration seemed to throw the other delegations into some confusion, although the French government later admitted that the declaration was a bargaining ploy, and that a final decision on secession will be taken later. Nevertheless, the council meeting passed a resolution which would enable other countries to withdraw at the same time as France, provided they announce such an intention by the end of June 1971. At the first council meeting last December, the French delegation refused to pledge full support for the programme of applications satellites, and this is one of the chief stumbling blocks that Dr Hocker must remove if he is to ensure that ESRO has a viable future.

CORROSION

The Price of Neglect

A NATIONAL Corrosion and Protection Centre should be set up to act as a focal point for all the knowledge and expertise at present spread rather unevenly throughout Britain. That is one of the chief recommendations set out in the report of the Committee on Corrosion and Protection (HMSO, 1971 ; 80p), and the committee adds that such a centre could be situated near an existing scientific establishment to make use of such facilities as a library and computer.

Set up in 1969 by Mr Anthony Wedgwood-Benn to survey all aspects of metallic corrosion and its prevention, the committee, under the chairmanship of Dr T. P. Hoar of the University of Cambridge, has produced a stark analysis of the total cost of corrosion and protection in the UK. This amounts to about £1,360 million per year. A close investigation of individual industries has revealed that about £310 million could be saved each year if more attention were paid to protection from corrosion—the total cost of corrosion is about 3.5 per cent of the gross national product in the UK compared with about 1.25 per cent in the US, for example.

Most of the saving could be made by increased awareness and improved information services on a national scale, the committee suggests, although the increase of knowledge about corrosion is obviously important. The cuts in corrosion costs which the committee thinks are possible in different industries vary widely from about 8 per cent for the oil and chemical industry to more than 40 per cent in the power industry. The very high value for the power industry reflects, in the committee's opinion, reluctance to make extensive use of cathodic protection methods for piping, and a worrying lack of knowledge at the design stage of equipment operating conditions. Government departments do not escape lightly and the armed services are criticized for lack of corrosion awareness among designers. The army owns many pieces of equipment, for example, which are stored throughout much of their life but must be ready for instant use and so have to be replaced from time to time because of corrosion.

Appropriate action at the design stage is the rule only in the aircraft and oil and chemical industries but in other sectors "attention to corrosion is largely confined to avoidance of bad mistakes made in the previous designs. This method of learning by trial and error is expensive and wasteful". The report also contains an assessment of the extent to which corrosion and protection are dealt with in educational courses of all kinds and comes to the conclusion that the training of engineers, designers and architects is generally deficient in anti-corrosion skills.

NUCLEAR ENERGY

Oil or Nuclear Power?

THE decision by the Central Electricity Generating Board to defer construction of the 2500 MW Sizewell B nuclear power station until at least 1972 and to go ahead during 1971 with an oil-fired station on the Isle of Grain flies in the face of those who were predicting that the recent oil price rises would swing the balance of argument firmly in favour of nuclear power stations, in spite of their higher capital cost. The construction costs of these two power stations are now estimated to be about £250 million and £200 million respectively, even though the capacity of the Isle of Grain station is about 25 per cent greater than Sizewell B.

The CEGB has based its decision ostensibly on the smaller annual rate of growth of demand for electricity which the Electricity Council now predicts for the next five years (5 per cent rather than 6 per cent). The peak demand of 54,000 MW which was anticipated for the winter of 1975 to 1976 is not now expected to be reached until the following year, and the board therefore argues that it is not necessary to start work on Sizewell B for at least a year. But it seems that the CEGB does not feel by any means committed to the Sizewell project even in 1972, in spite of an investment of more than £1 million in the preparation of the site. The board may see the trimming of its nuclear power programme as a way of meeting the cuts required in capital spending which will soon be spelt out by the Treasury. The fact that the capital cost accounts for about two-thirds of the total cost over an average lifetime for a nuclear station must certainly weigh heavily with the board in the prevailing economic climate; the proportion is nearer one-third for an oil-fired station.

The Sizewell B design contract was awarded to the Nuclear Power Group (NPG) last November and the decision to mark time on the project has sent quite a chilly wind through the whole British nuclear power industry. There seems little immediate danger of the NPG running short of work, however, because it is involved in the construction of two other nuclear power stations, Hinkley Point B and Hunterston B; these are both 1250 MW stations powered by advanced gas-cooled reactors—the same type as planned for Sizewell B. The NPG has also been careful not to rely entirely on nuclear power contracts and has, for example, the design contract for a 2000 MW oil-fired station at Inverkip on the Clyde.

COUNTRYSIDE

Power at the Top

THERE was evident satisfaction at the Countryside Commission when the chairman, Mr J. Cripps, announced on March 1 that the government had agreed to let the commission have a director at under-secretary level in the Civil Service. The change is more significant than it may seem. Mr Cripps was confident that an under-secretary will have more influence with ministers than the assistant secretary who has been the chief officer of the commission since its inception in 1968.

There can be no doubt that great things are expected of the new director, who is likely to be appointed in the next few weeks. The recent concession also includes a relaxation of Treasury control on expenditure. But the commission still has plenty of problems obstructing the full implementation of its job as the statutory national body responsible for matters relating to the conservation and enhancement of landscape beauty and amenity, and to the provision of facilities for the enjoyment of the countryside.

The greatest curb to the commission's activities is its lack of staff, and there seem to be no signs that the government will allow any increase in the near future. For this reason it is hoped that the officers of the commission will be consulted earlier in regional planning schemes so that some costly public enquiries can be avoided. Another grievance with the government is its decision to move the commission out of London. The commission does not want to go, saying that most of its business is transacted in London. The struggle will doubtless continue; meanwhile a nine months extension has been secured on the lease of the commission's headquarters at Cambridge Gate.

Parliament in Britain

Scientists' Unemployment

MR DUDLEY SMITH, Under-Secretary of State, Department of Employment, said that on December 2, 1970, there were 2,983 unemployed persons on the technical and scientific section of the professional and executive register. This figure includes 175 women. The information was given in reply to a question from Mr R. Carter. (Written answers, February 25.)

Abortion Act

A COMMITTEE of enquiry has been set up to review the workings of the 1967 Abortion Act. The enquiry will be concerned with the way the act is working and not with the principles that underlie it, and the chief conditions for legal abortion will remain unaltered. Announcing this in a statement given to the House of Commons, Sir Keith Joseph, Secretary of State for Social Services, also said that the government proposes to encourage the growth of local authority family planning services, especially in priority areas. Provision has therefore been made for expenditure on this service to treble by 1972-73.

Mrs Justice Lane will be chairman of the committee, and other members will be appointed later. The terms of reference of the committee are "To review the operation of the Abortion Act, 1967, and, on the basis that the conditions for legal abortion remain unaltered, to make recommendations." (Statement, February 23.)

Desalination

THE government is not yet ready to make a decision on whether to support construction of a pilot plant, situated at Ipswich, for production of desalinated water. Lord Sandford, Parliamentary Under-Secretary of State, Department of the Environment, said that the Secretary of State for the Environment should soon be able to come to a decision about the project. It would cost about £1.5 million. But Lord Kennett pointed out that when he was sitting in Lord Sandford's place nine months ago, before the election, he announced that the government was in the last stages of its consideration of the project. He therefore wondered why there has been such a delay in coming to a final decision. Lord Sandford replied that the government has been reviewing several schemes that were given the go-ahead by the previous administration, and he reaffirmed that a decision will not be long delayed. Lord Nugent of Guildford said that after a gestation period of nine months, there should be a reasonable prospect of providing an answer. (Oral answers, Lords, February 24.)

NEW WORLD

Sweetness and Light Break Out Again

by our Washington Correspondent

THE science policy making machinery in Washington is now running in perfect order, and the disharmony between its working parts that caused such discordances last year is already a distant memory, incapable of recurrence. This at least was the impression effortlessly given last week by the leaders of the various science policy making sections of government, between whom almost no trace of disagreement on any matter of substance was allowed to emerge. Among the auguries of this harmony is that the semi-increased budget of the National Science Foundation is assured of a reasonably comfortable passage through Congress. The only discordant note in the orchestra was the strident pitch made by the President's science adviser, Dr Edward E. David, on behalf of the SST.

David and other luminaries of government science officialdom were speaking at a seminar on science and public policy organized by the Council for the Advancement of Science Writing and held at the National Academy of Sciences from February 22 to 24. By far the most important utterances in the seminar were those of Congressman Edward P. Boland, making his first public appearance before the scientific community, over whose affairs the iron vagaries of the Congressional seniority system have now given him as powerful an influence as anyone in Washington.

As new chairman of the House appropriations committee that fixes the budget of NASA and the National Science Foundation, Boland will have a greater say in how these agencies operate than any members of the House Science and Astronautics committee or its subcommittee on Science, Research and Development. The latter committee has gained more public attention, particularly because of the hearings on many aspects of science policy conducted under its former chairman Mr Emilio Q. Daddario, but as an authorization committee its tangible effect on the funding of science is limited to setting an upper limit on the sum the house appropriations committee may appropriate for the NSF and NASA. Since the authorization committee seldom allows less for its agencies than the appropriations committee wants to give, the whip hand lies with the latter, and the only obvious restraint on an appropriations committee's will is that it must reconcile its differences with the counterpart committee of the Senate.

Boland's opinions on science and public policy, therefore, were listened to attentively, and although he gave no sign of the partisan fervour for science that everyone would like to see in an appropriations committee chairman, his attitude seemed at worst to be that of friendly neutrality. He complimented the director of the National Science Foundation, Dr William D. McElroy, calling him a "persuasive and diplomatic personality", and went on to observe that the NSF usually "gets about what it wants" in the appropriations process. McElroy will be particularly pleased if this reflexion turns out to apply to the NSF's 1972 budget under Boland's chairmanship since with a budget authority of $622 million ($116 million more than last year) the foundation has more than ever to lose at the trimmer's knife.

Although the NSF is only a small part of Boland's concern—his subcommittee also decides appropriations for the Department of Housing and Urban Development, NASA and a ragbag of smaller government offices—he has been a member of the subcommittee for some 16 years and appears well acquainted with the NSF's problems. He laughingly remembered the day when he was assured the foundation would never require more than $20 million a year for its support, but quickly set everyone's minds at rest by voicing his judgment that "the budget of the NSF will increase substantially in the years to come", chiefly to pick up the research being abandoned by other agencies.

Boland believes that responsibility for basic research is tending to become concentrated in the NSF although he sees serious dangers in the amendment tacked on to the military procurement bill by Senator Mansfield two years ago that set this trend in motion. "It seems to me that over the years the great breakthroughs we have had have come about because there has been basic research carried out by many agencies and many people. There may be duplication but this is not harmful. I think that when you have many agencies doing basic research there are more opportunities to acquire knowledge", Boland declared.

Boland's indications that the NSF would not get roughed up in Congress were followed by equally comforting assurances that science's two protectors in the executive are now at loggerheads no more. Mr William D. Carey, assistant director of the Bureau of the Budget (now the Office of Management and Budget) until 1969, told the seminar last week that there exists "a strong built-in disposition in the Office of Management and Budget for the support of science and technology. If the OMB could do what it wanted the hunger pains in the scientific community would never have been felt". The implication of Carey's remarks is that science might have retained its 15 per cent growth rate throughout the Johnson Administration were it not for another important factor in science funding, "the extent to which a sitting President has a glandular reaction to science and scientists" as Carey put it.

The honeymoon's ending was also soured by the attitude of the scientific community that all the favours given to them were no more than they deserved on moral grounds. "Don't blame the government for letting science down", Carey said. "The trouble was that scientists wanted to be rocked in a cradle, they didn't believe that summer was gone and winter coming". The chilliest part of the winter that ensued was when the Office of Science and Technology under Dr Lee Dubridge was locked out of the critical stage of preparing the President's budget, the directors' review meeting at which the final trade-offs are made. Carey observed that the OST and OMB are now friends again (if not yet, perhaps, the very good friends they were in his day) and that this year the OST was allowed back into the budget decision process. Nevertheless, relations have not been restored without price. Carey senses a change in the OMB's view of the National Science Foundation—"Instead of the NSF being regarded as a bottomless pit into which one dropped infinite sums of money without expecting even so much as a splash, the NSF today is being led closer towards the marketplace. When I dealt with the NSF there was a revulsion to tainting the NSF with any applied research . . . the present Administration has come to the decision that research ought to be guided towards pay-offs".

As if to bear out Carey's description of the applied role the Administration sees for science, Dr Edward E. David devoted the burden of his speech not to the state of science or intricacies of science policy but to saying how sad it will be if the supersonic transport is not built, at least in its experimental version. It is unusual for a President's science adviser to voice views so radically at variance with those of the scientific community on any issue, and to do so with such political partisanship. This perhaps is another part of the price paid for the OMB's friendship. David has once before entered the lists in support of the SST. After the debate on December 3 last year in which the scientific arguments against the aircraft weighed heavily in Senator Proxmire's victory over the Administration, David rounded up a list of no less than 30 scientists, including Dr Edward Teller, who put their name to a statement reproving the Senate for its action. "Our society must not suppress technological advances", David's scientists told the Senate, "but through research, development and experimentation make sure that those advances are obtained without undesired side effects".

David has now returned to the theme of suppression, but in interpreting the Senate's doubts about the desirability of the SST as signs that society has lost the will to experiment, he may have been carried a little beyond his audience's sticking point. The present situation, he said last week in a paper entitled "The Real Crisis", has led to "a loss of confidence by the public in the wisdom and objectivity of technical people, leading in turn to a loss of courage to authorize new experimentation or to undertake new innovative developments".

David went on to describe as the most serious concern for the nation the "increasing alienation of people in our society from rational ways of thought. I have listened to debates on the SST programme at some length", he added in explanation. Mentioning the *in vitro* fertilization experiments of Dr R. G. Edwards and his colleagues, which recently received some publicity before a Congressional committee, David implied that public concern was also impeding or about to impede biological experimentation. "There are many evidences that society does not believe that technology can be controlled in a rational way. Because of that, society is losing its courage to experiment. This trend leads to disaster, for it divorces our decision makers from reality. . . . Make no mistake, a limitation on experimentation in whatever cause is the beginning of a wider suppression. When we fail to experiment . . . we bring the best part of American society as we know it today to a halt. Already we see timidity in new undertakings. . . ."

The only serious aspect of this hyperbole is that next time a President's science adviser cries wolf on these grounds, nobody may listen to him. Under questioning, David was unable to cite any specific instance of society's "failure to experiment", other than the issue of the SST. Although adamant that he was pressing for construction only of the two experimental prototypes, David let it be known that a fleet of SSTs would help create the same kind of cultural links with Africa and Australia as conventional air travel has allowed to grow up with western Europe. "If we are going to forge a world-wide community in this sense, we may need to forge a new mode of travel", David explained.

Besides his advocacy of the SST, David had a few words on the unemployment situation—the OST estimates that there are 30–40,000 unemployed scientists and engineers, a rate of about 3 to 4 per cent. The government is tackling the problem by trying to provide placement and retraining services, by cutting back on the rate of increase of the pool of engineers and scientists, and by increasing the rate at which activity is shifted from defence and aerospace to civilian problems.

As for science policy, David said that the policy implications in the President's annual budget document were the product of a more coherent and consistent science policy programme than usually perceived by outside observers. Although more effort toward a science policy for US research and development is needed, David said, the chief problem is "somehow to avoid smothering the substance of science and technology by the inevitable doctrines and dogmas emanating from any science policy".

CONGRESS

Friend for Science?

by our Washington Correspondent

FOLLOWING a reshuffle in the subcommittee chairmanships of the House Appropriations Committee, Congressman Edward P. Boland has become chairman of the subcommittee on Independent Offices and Housing and Urban Development which decides the budgets of NASA and the NSF (subject only to an upper limit placed by the authorization committee). Although a member of the subcommittee for 16 years, Boland is not known to have any particular interest in science; up until now his energies have been concentrated on housing, public works and transportation.

The limit of the personal information Boland enters in the Congressional Directory is that he is the Democratic Representative of the second district of Massachusetts. The future wielder of almost absolute power over the budgets of NASA and the NSF is the son of an Irish immigrant from Fahan, County Kerry. A graduate of Boston College Law School, Boland was elected to the Massachusetts House in 1935 at the age of 24 and after three terms in the state house was elected Registrar of Deeds in Hampden County. Returning from war service in the Philippines, Boland is said to have refused $12,000 back pay (Massachusetts voted to award its office holders half their accumulated salaries) on the grounds that public officials were not a privileged class.

A Roman Catholic and unmarried, Boland was elected to the House of Representatives in 1953 and is now serving his tenth term. Although his constituency, including the town of Springfield, is in the west part of Massachusetts and out of the ambit of the east coast academic community, Boland is closely associated with the Kennedys, accompanied President Kennedy on his visit to Ireland, and during his administration had something of the status of an official spokesman in the House. He has voted in the main for traditional liberal measures, opposing the Sentinel anti-ballistic missile programme in 1968 and the proposal last year to expand the Safeguard system (as Sentinel has now become) to five sites. With 17 other Congressmen he sponsored a resolution in 1968, at a time when there were demands for another 200,000 men to be sent to Vietnam, to the effect that US forces there should not be increased without the explicit consent of Congress.

Boland's chief interests have been in the Model Cities programme, a piece of Great Society legislation under which federal support is provided to refurbish the physical and social milieu of selected cities, including Springfield, Massachusetts, as well as in transportation; he has been outspoken on matters of air safety and has served as chair-

Edward P. Boland.

man of the Appropriations subcommittee on transportation, a post he has now yielded. Boland's recorded pronouncements on space or science are few; in a speech made in 1958 in the aftermath of the launching of Sputnik, Boland declared that "in the present race for survival [the US] cannot afford to lose its vast reservoir of brainpower in the fields of engineering, science and the humanities merely because these young Americans cannot be given a college education".

But these are small crumbs of comfort for those seeking a commitment to science, since every Congressman was saying the same thing at the time. The indications from Boland's remarks at the CASW seminar last week are that he is well informed about science policy, favours a strong basic research effort by mission oriented agencies, and that if he has to wield the knife on NASA or NSF budgets will at least do so conscientiously.

NASA

A Leader Found

by our Washington Correspondent

WHEN a Dalai Lama dies the Tibetan priests search high and low for the newborn child whose features proclaim it to be the true successor to the Lama's throne. The Nixon Administration has been combing the land with equal care to find a successor to Dr Thomas O. Paine, who resigned as head of the National Aeronautics and Space Administration on September 15 to return to General Electric. The new head of the agency was announced this week after long delay and much vacillation in high councils as Dr James C. Fletcher, a 51-year-old Mormon who is president of the University of Utah.

The search for a successor seems to have been inhibited by the lack of appeal of presiding over NASA's contracting budget. At least eight people seem to have been considered with varying degrees of seriousness, including George M. Low, the deputy administrator; Howard W. Johnson, president of the Massachusetts Institute of Technology; Colonel Frank Borman; Congressman Richard L. Roudebush of Indiana; Roger Lewis, president of the General Dynamics Corporation; James M. Beggs, Undersecretary of Transportation; Congressman George Bush of Texas; and Frank Jameson, president of Teledyne Ryan Aeronautical.

Within the last few weeks the choice was narrowed down to Beggs, Jameson and Fletcher, and an article in *Business Week* for February 13 stated categorically that the job had gone to Jameson, described as a "real charger" of a man who would turn NASA to solving the national problems of education, ecology and the environment as well as keeping the flag flying in space. Unfortunately Jameson fell out of favour with the Lama-hunters in the White House before his appointment could be announced officially and after a few weeks of silence it emerged that the chosen one was not Jameson after all, but Fletcher.

Dr James C. Fletcher

Fletcher is a physicist with industrial experience in several aerospace companies. He served with the Aerojet-General Corporation prior to 1960, as president of the Space Electronics Corporation from 1960 to 1962, and as chairman of the Space General Corporation until 1964, when he became president of the University of Utah. Fletcher has also been a consultant to the President's Science Advisory Committee, the Office of the Secretary of Defense and the Arms Control and Disarmanent Agency.

Other recent changes in NASA's personnel include the dismissal at a month's notice of Julian Scheer, assistant administrator for public affairs, who has been with NASA since its earliest days. Architect of the extensive coverage whereby NASA's doings were made known to the world, Scheer is said to have fallen foul of certain congressional interests in his methods of presenting NASA.

ARMS RACE

Accuracy of ICBMs

by our Washington Correspondent

AN order of magnitude improvement in missile guidance is within the grasp of present-day technology, according to Dr David Hoag, director of the Apollo Guidance and Navigation Program. Quite feasible advances in missile guidance techniques could reduce the average error with which an ICBM hits its target, now 1,000 metres at most, to about 30 metres, the chief residual source of inaccuracy being imperfect knowledge of the Earth's gravitational field.

Improvement of missile accuracies to this degree has alarmed many arms control experts because of the possibility it offers of a successful first-strike attack that would destroy the enemy's missiles in their silos. Hoag, however, in a paper delivered to a Pugwash symposium held at Racine, Wisconsin, last June and now published in book form* argues that the development of high accuracy missiles would encourage the exchange of weapon against weapon instead of weapon against city.

Hoag lists seven major sources of inaccuracy in missile guidance and the approximate errors they cause in the range and track of the missile. One class of error resides in the inertial sensing caused by errors in the accelerometers and gyroscopes. Another may be inaccuracy in specifying to the missile's computers initial conditions such as the location and attitude of the missile on its launcher. A third kind of error may arise from the computations used to track and control the missile's flight. By and large, the trajectory calculations can be made as precise as desired by increasing the number of terms in the power series describing the trajectory, which is limited only by the capability of the on-board computer. Hoag believes that the state of technology in compact digital computers should be able to reduce target-miss contributions from this source to negligible proportions.

Thrust termination errors arise if all the components of the missile velocity fail to attain the exact value required at the moment the rocket thrust is cut off. For example, a 0.1 metre/sec difference between actual and predicted values causes a 650-metre miss at the target. This difficulty can be eased by using an additional low-thrust rocket, called a vernier stage, which adds the last small part of the required velocity. In fact, for a MIRV missile the final vernier-like correction can be made as the individual warheads are released from their "bus".

Fifth, there are the gravity anomalies in the Earth's gravitational field which are too slight to affect missiles at full height but may exert a small influence during the initial and terminal phases of flight. A gravity anomaly altering a missile's velocity by 0.02 metre/sec during the first 100 seconds of launch could cause a 50-metre miss at target.

Uncertainties in the geographical coordinates of the target are a sixth source of error, and finally the missile may be deflected by aerodynamic forces as it re-enters the atmosphere.

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* *Impact of New Technologies on the Arms Race.* Ed. B. T. Feld and others. MIT Press, 1971; $2.95.

NEWS AND VIEWS

Polywater Drains Away

It now begins to seem as if the concept of polywater is on its last legs. The article by Barnes, Cherry, Finney and Petersen on page 31 of this issue of *Nature* is one of several recent demonstrations that many of the observations put forward in the past few years as evidence of the existence of an anomalous form of water must be accounted for quite differently and much more trivially. On the face of things, at least, polywater seems to be not a distinct, stable (or metastable) form of water, but water contaminated by various substances among which silicates seem to be conspicuous. One of the most striking and direct demonstrations of this was the article by Bascom, Brooks and Worthington last year (*Nature*, **228**, 1290; 1970), which described how electron probe measurements of the residues obtained by condensing polywater had revealed the presence of silicon and sodium atoms. The quantities are indeed sufficiently small to explain why the presence of impurities has been unnoticed for so long. This, however, does not fully account for the way in which experimenters in the late nineteen sixties were apparently happy to record observations of anomalously high viscosity and boiling point without subjecting their samples to the full rigours of modern microanalysis.

The social significance of this phenomenon is important for the conduct of science as a whole. This, after all, is not the first occasion on which groups of people have been led astray in the pursuit of physical phenomena which later turn out to be unreal. At the turn of the century, for example, there was a great fashion for the study of "N-rays" as they were called, supposed accompaniments of some forms of radioactive decay. All kinds of reputations were then pinned to the characterization of a phenomenon that turned out to be an illusion. On reflexion, of course, it is ironical that soon after the false doctrine of N-rays had flourished and then disappeared, biologists fiercely resisted the suggestion that some forms of chicken sarcoma could be transmitted by the so-called Rous sarcoma virus. It has taken a long time to show that this scepticism was misapplied. The problem of polywater is more subtle, to the extent that the growth of the concept has required not merely the suspension of belief or disbelief but an unwarrantable restraint on the use of observational techniques which are, after all, familiar enough. The failure of several experimenters to pursue with all the vigour at their command the possibility that contamination might account for most of their observations is nothing to be proud of.

So has the rise and fall of polywater been nothing more than a salutary lesson for everybody, theoreticians as well as experimentalists? Luckily, even unhappy tales like this contain the seeds of useful and constructive speculation. Thus there has been great interest in model building with water molecules, and many theoreticians have been led to construct schemes for estimating the severity of three-dimensional complexes of water molecules which are of great interest in themselves. If, as now seems likely, the properties of polywater are to be explained away by the presence of similar atomic networks in which atoms of silicon play a part, it remains something of a surprise that sheets of atoms constructed in this way can serve so dramatically to modify bulk properties such as viscosity and boiling point.

The DNA Replication Mystery

As a group, molecular biologists have never fought shy of publicity and their propagandists have fed the popular image of the juggernaut subject advancing by enormous strides on all fronts. All fronts bar one, which is usually glossed over; for, although anybody reared on the current rash of molecular biology texts might be excused for thinking otherwise, the precise mechanism by which DNA is duplicated is almost as obscure today as ever.

To be sure, in the nineteen sixties Kornberg and his collaborators isolated from *Escherichia coli* an enzyme which can polymerize DNA and, for example, replicate infectious bacteriophage DNA *in vitro*. And until last year this enzyme, DNA polymerase I, was the only known enzyme with this capability. Small wonder therefore that many molecular biologists bent over backwards devising all sorts of ingenious schemes to explain how it might replicate DNA *in vivo*. But they laboured under one great disadvantage and probably in vain, for the properties of polymerase I (it makes DNA very slowly, it can only synthesize DNA in one, the 5′ to 3′ direction, and it is an effective exonuclease) are those expected of a DNA repair enzyme rather than a replicase. In other words, polymerase I has all the properties of an enzyme which edits DNA sequences, excising regions of mismatched base pairs and replacing them with the correct sequence, rather than replicates them.

The days of tortuous scheming are, however, over; the pressure is off polymerase I for two related reasons. First, at the end of 1969 De Lucia and Cairns isolated six mutant *E. coli* which lack or contain defective polymerase I but nonetheless survive and replicate their DNA normally. Second, several groups have detected and begun to isolate a second DNA polymerase, polymerase II, in these mutants. With at least two candidates at last in the lists, those molecular biologists concerned with defining the mechanism of DNA duplication are currently far more intent on characterizing DNA polymerase II and searching for further species of DNA polymerase than on striving to accommodate polymerase I in hypothetical schemes of DNA replication. Few of them would now quarrel with the statement that the chief and probably sole function of polymerase I is DNA repair. If there are any waverers still sitting on the fence they should be finally decided by what Kelley and Whitfield have to say, on page 33 of this issue of *Nature*, about one of the six mutants isolated by De Lucia and Cairns.

De Lucia and Cairns, when they began their mutant hunt, argued that if polymerase I is a repair enzyme it should be possible to select mutant *E. coli* with a defective repair mechanism, because of a defective polymerase I, but still capable of normal DNA replication. They proved their point by isolating six such mutants, the first of which to be characterized proved to be an amber mutant. But although these strains lacked polymerase I activity and were unusually sensitive to ultraviolet light, there was no proof that the mutations were actually in the structural gene which specifies polymerase I. It might, for example, still be argued that the mutations were in a regulatory gene and result in a drastic reduction in the amount of polymerase I made. If that were the case, the handful of perfectly normal polymerase I molecules might all be sequestered immediately for DNA replication, which would proceed normally, leaving none available for DNA repair.

Because of such arguments it became a matter of considerable importance to find proof that any one of the six mutants De Lucia and Cairns isolated (all those mapped so far are in the same gene) contain a lesion in the structural gene directly specifying polymerase I. For, clearly, if the enzyme molecule itself contains a mutation which reduces its capacity to polymerize DNA, and cells containing such mutant enzyme replicate their DNA but lack a repair mechanism, the straightforward conclusion is that the polymerase I is involved in repair but not replication. Of course, anybody absolutely determined to keep all options open could say that all the mutations by chance occur in that part of the polymerase I molecule, admittedly a large protein comprising about 1,000 amino-acids, which is involved in repair, leaving the part responsible for DNA replication intact. But that is surely less plausible.

Fortunately as Kelley and Whitfield have now convincingly shown, *pol 6*, one of the half dozen mutants, turns out to be a temperature sensitive mutation. They purified polymerase I from this mutant and wild type *E. coli* and compared the properties *in vitro* of the two enzymes. The wild type enzyme has the same activity at 37° C and 52° C and its optimum temperature is 55° C. By contrast the mutant enzyme had less activity at 52° C than 37° C and an optimum temperature of about 45° C. Further, the two enzymes differ in their response to various synthetic DNAs and, although immunologically similar, sensitive complement fixation tests at various temperatures indicate that they differ in precise conformation. In short, the *pol 6* mutation is in the structural gene specifying the enzyme. Polymerase I is therefore certainly involved in DNA repair, and although it is premature to state categorically that that is the enzyme's sole function, the odds are stacked very high against the idea that polymerase I has a role in DNA replication.

What Turns Plants On?

By the late 1950s, it seemed clear that there is a subtle—at that time, many privately thought mythical—pigment system located within the plant which can differentiate between light and dark; a mechanism which can be "switched-on" by daylight and "switched-off" by the approach of nightfall. In 1959, the doubts of even the most sceptical of biologists were stilled when W. L. Butler and his colleagues at the United States Department of Agriculture Research Station, Beltsville, Maryland, used a modified difference meter—a machine derived from the Chance spectrophotometer and designed originally to test for ripeness of fruit—to demonstrate the physical presence of the pigment phytochrome in plant tissue. Since then, phytochrome has been extracted from a great variety of plant material. It has been partially purified, and has been shown to be a blue-green chromoprotein, perhaps rather similar to the algal chromoprotein allophycocyanin.

At present, opinion is sharply divided about the exact mechanism of phytochrome action. On one hand, the Beltsville group have proposed the activation of some cellular metabolite or membrane component. In an article published last year in *Nature*, Harry Smith extended this idea to suggest that phytochrome might be located within certain critical membranes, and that its function might be that of a transpermease; a molecule responsible for ferrying important metabolites across the membrane (*Nature*, **227**, 665; 1970). On the other hand, for some years now Hans Mohr and his group at Freiburg have been assembling data to support the idea that phytochrome, when switched on by light, activates specific genes which had been only potentially active while the plant remained in darkness. The enzymes formed as a consequence of this gene derepression are then responsible for initiating the structural changes which mark photomorphogenic development in the light.

There is good evidence to support both of these ideas, and very little to suggest that either hypothesis should be discarded. What Professor Mohr proposes on page 56 of this issue of *Nature* is not a new scheme to explain the mechanism of phytochrome action, but the equally valuable suggestion that there is now enough experimental evidence to indicate to plant physiologists that they must be less rigid in their way of looking at the problem of photomorphogenesis. In particular, he asks, what justification is there for the widespread assumption that the primary reaction of phytochrome—the first reaction in which the phytochrome molecule participates after its activation by light—is the same in all plant species, all cell types and in all parts of the same cell?

The idea that there is but one primary reaction in the phytochrome system must have sprung originally from the vast range of plant photoresponses in which the pigment is implicated. These include time dependent responses—flowering, circadian rhythms, re-setting of the biological clock—and time independent responses—pigment formation, enzyme synthesis, de-etiolation, tropisms. All of these responses involve a large amplification factor, that is, the amount of light energy required to initiate the process is small compared with the energy required for the final display. It seemed likely therefore that phytochrome must act at some very early common point in the metabolic processes causing these phenomena. Professor

Mohr has now re-examined his data for the phytochrome regulated synthesis of anthocyanin and ascorbic acid in the white mustard seedling, using sequential irradiations with red and far-red light. Briefly, red light promotes the formation of the apparently active form of the phytochrome molecule, PFR, and thereby initiates biochemical synthesis. Far-red light, however, abolishes this response by converting PFR back to the inactive form of the molecule PR. In continuous far-red light, however, enough phytochrome is converted to PFR to initiate and maintain the synthesis of anthocyanin and ascorbic acid. This property of the phytochrome molecule makes it possible to perform some pretty tricks with red and far-red light. The way the plant reacts to these colours of light given in different amounts and in different sequences makes it possible to gain some insight into what the phytochrome molecule is doing in the cell.

Mohr and his colleagues show that in continuous far-red light, PFR exists in an, as yet, unexplained "excited" state, which promotes the formation of both anthocyanin and ascorbic acid. With the passing of time, however, it becomes clear that this "excited" state is not the same for the two synthetic systems. After twelve hours of continuous far-red light, red light greatly promotes the synthesis of anthocyanin, but is completely ineffective in promoting further synthesis of ascorbic acid. What Mohr deduces from these results is that the PFR formed under far-red light takes part in different kinds of primary reactions in promoting synthesis of the two compounds. In one case the molecule is still susceptible to further conversion by red light, but in the other the active molecules have become in some way immune to further photoconversion.

Important and unequivocal as this conclusion is, there will inevitably be much head shaking and anguish in the photomorphogenesis camp. The attempt to isolate one primary reaction for phytochrome has proved challenge enough; what hope is there of identifying similar involvements? There is not much hope at present, perhaps, but at least Mohr's conclusions should make it rather simpler to explain those paradoxical experimental results where the behaviour of phytochrome as observed in the difference meter seems to bear no relation at all to the physiological responses of the plant.

EXPLORATION

Sacrifice for Plants

by our Botany Correspondent

WHATEVER may be said about the boredom of botany, its exponents used to be among the most reckless of adventurers, facing disease and danger in the search for new knowledge. Among the most intrepid of plant hunters were Sir Joseph Banks and Daniel Solander who sailed to Australia two hundred years ago with Captain James Cook on his ship Endeavour. The plants which they collected on this voyage became the basis of the department of botany of the British Museum (Natural History) where they are still in constant use. Banks's great contribution to botanical knowledge was recalled on February 23 by Dr W. T. Stearn when he gave the second of six weekly lectures about the Natural History Museum, which have been sponsored by the museum and the Victorian Society.

Banks, a rich landowner who had been to Eton, Harrow and Oxford, showed sufficient promise as a botanist to be elected a Fellow of the Royal Society at the age of 23. Deciding that a trip to the South Seas would provide a good opportunity for a grand tour of the world, he persuaded the society to let him go with Cook on his voyage to observe the transit of Venus. Banks also enlisted the Swede Daniel Solander, an extremely erudite pupil of Linnaeus, and Sydney Parkinson, the artist who died during the voyage.

The first important collections of the voyage were made during secret midnight excursions at Rio de Janeiro, where the Portuguese viceroy would not let Cook and his men ashore. In Tahiti, where the welcome was much more friendly, they found a rich vegetation, especially orchids, but Banks was most impressed by the breadfruit plant. From Tahiti, where the transit of Venus was duly observed, the expedition moved south, and, not finding the great southern continent which some people had imagined to be there, pressed on to New Zealand. Here a large collection of specimens was assembled, including the shrubby veronica, *Hebe*. Banks's foresight in taking along a Tahitian priest who could act as interpreter enabled the explorers to make friendly contact with the Maoris, who had attacked their previous European visitor Abel Tasman.

Endeavour then proceeded to Australia, known then as New Holland, the west side having been explored by the Dutch. Cook and his comrades found an inlet on the eastern coast which the captain would have called Sting Ray Bay, but which was so rich in floral delights that it was named Botany Bay. *Acacia* and the shrub which was later to be called *Banksia* were two of the many plants they found there. After leaving Botany Bay, Endeavour struck a coral reef and had to put into a nearby river inlet for repairs.

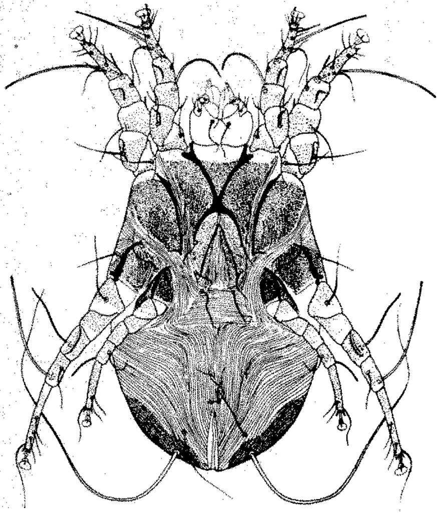
At the end of six weeks when the work was complete, the botanists had become familiar with every aspect of the surrounding flora and fauna. They saw a kangaroo, which was then unknown in Europe, and was to be classified by a German scholar as a new species of mouse, *Mus kangaroo*. Dr Stearn visited this part of Queensland last year, and found its vegetation virtually unchanged from the descriptions of Banks and Solander. He advocates that this region around Cooktown should become a new national park.

After many privations, particularly in disease ridden Java, where Parkinson and other crew members died, the survivors arrived home, and Banks established his home in London as a scientific centre. Sadly, the book he had planned as a record of the voyage, to be illustrated by Parkinson's drawings, was never finished. But his collections passed to his colleague Robert Brown, an army surgeon turned botanist, who added to them during his own travels. Brown, whom Dr Stearn described as the greatest botanist Britain has produced, went on the next British voyage to Australia, which was led by Flinders. He was accompanied by the Viennese artist Ferdinand Bauer, and they brought back a wealth of specimens and drawings. At the same time, Bauer's brother Franz settled at Kew, where a collection was growing up to rival that started by Banks, Brown gave his collections to the British Museum and became the first keeper of the department of botany, from which was to grow the separate Natural History Museum.

Chaitaea tacca (*Tacca leontopetaloides*) collected from Tahiti and drawn by Parkinson in 1769. The drawing is now in the department of botany of the British Museum (Natural History).

ACAROLOGY

Banana Mite



Eight specimens, all female, of an unknown species of mite were collected in 1968 from some bananas in Guatemala by Dr D. Johnson, of the US Department of Agriculture. These mites have since been examined by Dr A. Fain (Institut de Médecine Tropicale, Anvers) and Dr G. W. Wharton (Ohio State University) who conclude that they belong to a new genus and species of the subfamily Dermatophagoidinae (*Bull. Inst. Roy. Sci. Nat. Belg.*, **46**, No. 27; 1970). So far only the female of the species is known. This figure shows the ventral view of the new mite, *Guatemalichus bananae*, the body of which measures 450μ by 293μ.

RIBOSOMES

Protein Count

from our Molecular Biology Correspondent

THE perennial question whether all ribosomes in a cell are alike or differ in their protein composition rears its head yet again. Voynow and Kurland (*Biochemistry*, **10**, 517; 1971) earn admiration for their perseverance in examining once more the stoichiometry of the 30S *Escherichia coli* ribosome. They have noticeably modified their position as stated in their paper of last year, though the presence of one molecule in each particle of at least a large number of the twenty-one recognized ribosomal protein species remains unchallenged.

Two procedures have been used for estimating the relative concentrations of labelled protein components separated by electrophoresis in polyacrylamide gels. One is direct counting of the sliced gel, and the other, which is advantageous for incompletely resolved components, is an isotope dilution method involving the addition of single prepurified proteins, in known concentration to the mixture before electrophoresis. The two methods give good enough agreement but the interpretation of the results leaves room for a fairly generous element of personal preference. The reason is obvious enough; the ribosome will tend to pick up any basic proteins with which it chances to come into contact, for example after lysis of the cells. Such externally adsorbed species can be removed by washing with solutions of moderately high salt concentration, but at some point, or perhaps progressively, ribosomal proteins—those that reside and function in the ribosome *in vivo*—will also be extracted. The treatment that Kurland and his colleagues have used to purify ribosomes tends to the severe, as Voynow and Kurland now implicitly concede. The ambiguity is partly resolved by a comparison of the content of individual proteins of their scrubbed ribosomes, and what they refer to as crude—or, as some other workers would suggest, undamaged—ribosomes.

Referring to washed ribosomes, Voynow and Kurland divide the eighteen proteins that they are able to separate into three categories—unit proteins, which are present to the extent of one molecule per ribosome, fractional proteins, and those on which they are not prepared to commit themselves. There are only six in the first group, but seven in the second. In the unwashed ribosomes at least two of the latter are present in molar proportion. The most satisfactory feature of the results is that the six unequivocal unit proteins are Nomura's core proteins, which are all indispensable for the correct assembly of the 30S ribosome from its constituents. There are no proteins present to the extent of more than one molecule per ribosome.

In favour of the view that certain proteins are indeed present only in some of the ribosomes is the numerological argument, whereby the sum molecular weight of the twenty-one proteins and the 16S RNA is above the accepted value for the molecular weight of the 30S ribosome—though this again plainly depends on the manner of washing.

Light on the same problem comes from the work of Warner on the kinetics of assembly *in vitro* of the 80S ribosomes of yeast. He finds (*J. Biol. Chem.*, **246**, 447; 1971) that all the proteins in the 40S subunit are between 10,000 and 30,000 molecular weight, whereas in the 60S subunits they range up to about 46,000 (as estimated by detergent-acrylamide gel electrophoresis). With a pulse label, after a two-minute interval, the electrophoretic pattern of radioactivity shows some quite gross differences from that after 40 minutes, indicating either that the pool sizes of different ribosomal proteins differ markedly, or that there is a transient difference in the distribution of proteins in the cytoplasmic ribosomes. Evidence in favour of the second explanation comes from experiments with temperature-sensitive mutants grown at restrictive temperatures, which still show the emergence of the transient rapidly labelled components. As in other eukaryotic systems the newly synthesized ribosomes appear in the cytoplasm as subunits, and are only after a long interval, associated perhaps with uptake or loss of proteins, incorporated into polysomes. Warner suggests that the changes with time in the distribution of protein components of the ribosome may well reflect functional entities such as protein synthesis "factors", or for that matter fractional proteins such as those of *E. coli*.

Heterogeneity of Normal Fibrinogen

THE recognition of the existence of genetic variants of clotting factors VIII, IX, X and fibrinogen is of profound importance in the study of blood coagulation. Most clotting factors, with the exception of fibrinogen, are present in only trace amounts in plasma and the finger printing of fibrinogen molecules is a necessary prerequisite to the study of other clotting factors, at the molecular level.

The article by Gaffney in next Wednesday's *Nature New Biology* provides additional evidence for the heterogeneity of normal fibrinogen. Using acrylamide gel electrophoresis of the unmodified fibrinogen they obtained only a single band but, after sulphite cleavage of the fibrinogen, separation with the α (A), β (B) and γ chains was effected. The three chains of sulphitolysed single donor and pooled fibrinogens were subdivided further into discrete bands with the new technique of isoelectric focusing (IEF) acrylamide. The sulphitolysed fibrinogen from a single donor gave fewer bands of differing intensity and location.

This is not the first piece of work which suggests the existence of different normal fibrinogen molecules, and the author's previous work on prolonged plasmin digestion of single donor fibrinogen provides supporting evidence (Jamieson and Gaffney, *Biochim. Biophys. Acta*, **154**, 96; 1968). These techniques are less definitive than the finger printing techniques of Blomback *et al.*, who demonstrated an amino-acid substitution and deletion in the α chains of normal fibrinogen (*Nature*, **218**, 130; 1968). Blomback *et al.* also showed that the N terminal part of the α (A) chain of the abnormal "fibrinogen Detroit" had arginine residue 19 of a normal α (A) chain replaced by a neutral amino-acid, probably serine (*Nature*, **218**, 134; 1968). It will be of interest to study the IEF acrylamide pattern of several single donor normal fibrinogens after sulphite cleavage as an aid to polymorphism studies.

CHEMICAL CARCINOGENS

Smog Transformations

from our Cell Biology Correspondent

CONSERVATIONISTS, especially those whose chief concern is urban air pollution, should read the latest issue of the *Proceedings of the US National Academy of Sciences* (**68**, 445; 1971). Huebner's group report that extracts of city smog induce the transformation of rat cells infected, but not transformed by mouse leukaemia virus, hamster cells carrying the so-called hamster leukaemia virus and hamster cells apparently free of any tumour virus. Their concluding remark, "a relatively small volume of smoggy urban air may contain a tissue culture transforming dose of smog residue", is of the sort which will be widely aired no doubt in the forthcoming battles over cleaner automobile engines.

It is well known that urban air contains carcinogenic materials but, in the past, assays for these substances have been tediously slow because they have involved painting smog extracts on mice or other suitable animals and waiting for a tumour to develop. The advantages of the *in vitro* assay Huebner and his colleagues have devised are that it is quick, comparatively inexpensive and sensitive. In essence they have exploited their earlier finding that certain chemical carcinogens act synergistically with tumour viruses. A cell exposed to both virus and carcinogen is transformed whereas exposure to either virus or carcinogen alone does not result in transformation. Having filtered some 1.1×10^7 m^3 of air from what they discreetly describe as "a central location in one of the major metropolitan areas of the United States", Huebner and his colleagues extracted with benzene from the filters a residue, the concentration of which in air is about 16.2 $\mu g/m^3$. Each gram of this residue contained the equivalent of about 23 µg of benzopyrene (BZP) and the doses used in the experiments were therefore measured in unit equivalents of pure benzopyrene.

Cultures of rat embryo cells free of leukaemia virus were not transformed by doses of smog residue up to 0.007 µg BZP units/ml., neither were they transformed by doses of up to 1.0 µg/ml. of pure benzopyrene. Cultures of similar cells infected but not transformed by Rauscher murine leukaemia virus were, however, transformed after exposure to doses of residue as low as 0.0007 µg BZP units/ml. Essentially similar results were obtained in similar experiments with hamster cells carrying hamster leukaemia virus. Furthermore, cultures of hamster cells free of any RNA tumour virus were also transformed by doses of 0.007 µg BZP units/ml. but not by doses ten-fold less concentrated.

As Huebner and his colleagues note, the smog residue contains some transforming agent about six hundred times more efficient than pure benzopyrene. They also point out that the transformed cells produced by exposure to smog residue have not so far induced tumours when transplanted into suitable recipient animals and the results of their *in vitro* tests have yet to be correlated with a demonstration that the residue is carcinogenic for intact animals. Assuming, however, that that will be done, their procedure promises to be a useful method for assaying the carcinogenic potential of chemicals from a variety of sources as well as smog.

NUTRITION

Asian Diet

from a Correspondent

SINCE the first international congress of nutrition was held twenty-two years ago, the successive triennial meetings have become larger and broader in scope. Smaller meetings, dealing with the more specialized problems of a geographic region or of a particular aspect of nutrition, have therefore become increasingly popular. The most recent of these, the First Asian Congress of Nutrition, held in Hyderabad from January 27 to February 3, was also the first at which the related themes of nutrition and of national development were discussed against the background of high population density and almost universal dependence on cereals as sources of both protein and calories, which typify this portion of the developing world.

In order to formulate a nutrition policy, a correct diagnosis of the nature of the nutritional problems of a country is obviously essential, and much lively discussion at the meetings centred around the implications of the most recent estimates of the requirements for protein of the vulnerable groups of the population,

Ribosomes of Mouse–Hamster Hybrids

HYBRID cells, obtained by inducing with inactivated Sendai virus the fusion of two or more different cells, are proving to be extremely useful material for investigating the control of gene expression in animal cells. The latest example of their exploitation to this end appears in next Wednesday's *Nature New Biology* in which Stanners, Eliceiri and Green describe the analysis of the ribosomes in mouse–hamster hybrids. In extracts of the cytoplasm of these hybrids they have found both hamster and mouse ribosomes. This situation is in marked contrast to their previous findings that mouse–human hybrids contain only murine ribosomal RNA even though the particular hybrids they studied retained as many as thirty-five human chromosomes including those believed to carry the genes which specify human ribosomal RNA. Taken together, the new and old data indicate that it is unwise to generalize about the pattern of expression and repression of the mixed genomes in hybrids.

Human and mouse ribosomal RNAs can be distinguished by their different electrophoretic mobilities. Hamster and mouse ribosomal RNAs, by contrast, have more or less identical electrophoretic mobilities, and therefore Stanners and his colleagues had to search for some other criterion to distinguish mouse and hamster ribosomes. They have exploited Reader and Stanners's observation that hamster ribosomes, not actively translating a messenger RNA, tend to form dimers whereas free mouse ribosomes remain monomers. The question of whether or not hamster ribosomes are made in mouse–hamster hybrids boils down simply to an analysis of the occurrence of monomeric and dimeric free ribosomes in the hybrid cells.

It turned out that the hybrid cells yielded both monomeric and dimeric ribosomes. Further, the dimers could be disaggregated by heating to 37° C, but when cooled to 0° C they reassociated to yield dimers but never any larger aggregates. Working on the assumption that the dimers are indeed hamster ribosomes, Stanners and his colleagues tried to establish whether dimerization occurred through the ribosomal RNA rather than the ribosomal protein. If the former is the case all the RNA in the dimers should be hamster specific and by labelling parallel cultures of the hybrids with ^{14}C or ^{3}H uridine Stanners *et al.* have been able to confirm that, allowing for cross contamination, all the 28S RNA in the dimers is indeed hamster specific. They have also shown that a 40S RNA can be extracted by appropriate techniques from the dimers. This RNA is, they believe, a complex of two hamster 28S RNAs, into which it can be dissociated.

In short it seems that free hamster ribosomes are able to form dimers because of an affinity between the 28S hamster ribosomal RNAs; furthermore, the observation that aggregates of more than two hamster ribosomes are never found suggests that each 28S RNA contains only one dimerization site. In mouse–hamster hybrids, transcription of the ribosomal RNA cistrons is not restricted to those of only one parent. It would be interesting to know whether there is any preferential transcription of ribosomal RNA cistrons in hamster–human hybrids and in other hybrids obtained by fusing hamster cells with cells of other species. The curious phenomenon of dimerization of hamster ribosomes is clearly going to provide a simple marker for studying the synthesis of species-specific ribosomal RNAs in many different types of cellular environment.

and of the metabolic interrelationships between protein and energy utilization in the body. Thus, Dr P. V. Sukhatme (Food and Agriculture Organization, Rome), in reviewing estimates of food consumption in relation to income, drew the conclusions that, first, malnutrition is chiefly associated with poverty, that is to say with an uneven distribution of food resources within communities rather than an overall deficit of production at the national level; second, that the major deficiency in India and most other Asian countries is that of calories rather than of protein; and third, that food and nutrition planning should aim at eliminating the deficit by improving both the supply and distribution of foods of the same kind as are currently being eaten. The cereal–pulse based diets of the region are sufficiently well balanced in respect of their protein and amino-acid contents to meet the requirements of infants during the transition from breast feeding to a solid diet. This diagnosis, based on the intakes of food by households, was supported by a review by Dr Ambalini Bailur (National Institute of Nutrition, Hyderabad) of individual intakes of more than 30,000 pre-school children in six regions of India. In all cases, the diets eaten contained an adequate proportion of protein making due allowance for its quality, but the amounts eaten were inadequate to meet energy needs in 92 per cent of the children.

The prospects for improving the nutritive value of food grains were discussed by Dr M. S. Swaminathan (Indian Agricultural Research Institute, New Delhi). Level of yield, of protein and of lysine content can all be influenced by genetic selection. Thus the scope of the "green revolution" can be extended both by these techniques as well as by the adoption of varieties that lend themselves to multiple cropping.

The complexity of the interrelationships between nutrition and infection was reviewed by Dr N. S. Scrimshaw (MIT, Cambridge, Massachusetts). Experience in Guatemala has emphasized the need for an integrated approach to nutrition and public health programmes.

In developing countries, where resources are limited, a clear assessment of priorities is an essential prerequisite for the formulation of nutrition policies. The problems involved in this were discussed by Dr J. L. Joy (University of Sussex), who stressed the need for a re-examination of the nutrition problems of developing countries, which should be seen as caused not so much by deficits in the supply of food either in respect of quantity or quality, but rather as the result of inequalities in the distribution of demand (purchasing power) or of resources (land, water and the like) among the population. An increase in total food production may be necessary for improvement of nutrition, but by itself will never be sufficient.

POLLUTION

Problems with SO_2

from our Geomagnetism Correspondent

THE obvious way to reduce atmospheric pollution is to cut the pollutants off at source—cut down the pollutants by half, perhaps, and the pollution will be halved likewise. But if a recent study by Golden and Mongan (*Science*, **171**, 381; 1971) is anything to go by, this apparent truism turns out to be a gross oversimplification. A study of atmospheric diffusion over Cook County, Illinois, has shown that although electric power plants burning fossil fuels contribute about 78 per cent of the sulphur dioxide emission into the atmosphere, they account for only 14 per cent of the sulphur dioxide at ground level. It follows that the complete elimination of power plants, or at least the complete elimination of their SO_2 emissions, would make little difference to the exposure of the population to this corroding chemical.

The basis of Golden and Mongan's analysis is a model—the Air Quality Display Model (AQDM) developed by the National Air Pollution Control Administration—and to this extent it rests on assumptions which are not easy to verify. On the other hand, it is a tried and tested model. The AQDM permits the calculation of annual average concentrations of contaminant at specific points at ground level as well as the percentage of the concentration contributed by each point or area source. When these calculations were made for data from Chicago, for example, the results were reasonably consistent with observed concentrations of SO_2 during 1968. Golden and Mongan are thus convinced that the model is a good first approximation in areas with level topography and so should give sensible results for Cook County.

Why then do power plants contribute so little of the SO_2 concentration at ground level? Ironically, it all seems to be the result of a primitive pollution control measure adopted many years ago before pollution became the matter of great public concern it is today—the tall chimney stack. The whole object of the tall stack is to avoid high concentrations of SO_2 and other pollutants in the vicinity of the power plant by diffusing them over a wide area and by ensuring that they are highly diluted before reaching ground level. Of course, there is always the possibility that unfavourable meteorological conditions will occasionally defeat the object of this exercise. For this reason the power plant is likely to remain an important target for control. Unusual conditions apart, however, it should be possible to site power plants within a given region in such a way that the yearly average concentration of SO_2 at any given point is lower than the maximum considered desirable by the community in question. Where human health is concerned, Lave and Seskin (*Science*, **169**, 173; 1970) have concluded that "it is the minimum level of air pollution that is important, not the occasional peaks". The power plant

Magnetic Fields in the Crab Nebula

THE nature of the magnetic fields revealed by the structure of the Crab Nebula is of great interest, because of the link between these fields and the underlying pulsar. There is no other known system which contains a pulsar young enough for the gases left by the supernova in which it was created to be still visible, so the Crab offers a unique testing ground for pulsar models. Last January, Forman and Visvanathan offered an interpretation of the way in which light coming from this nebula is polarized. They found a smooth variation in this polarization (*Nature*, **229**, 39; 1971), but in next Monday's *Nature Physical Science* J. D. Scargle, who has been associated with observational measurements of polarization in the Crab, points out that interpretation of these data must be approached with great care.

The chief difficulty affecting the observations is the different thickness of nebula in the line of sight at different distances from the centre—assuming a spherical distribution, light is seen from a much greater quantity of gas when the centre of the gas is looked at closer than the edge.

Scargle suggests, however, that the observations show a roughly elliptical cavity immediately around the pulsar, just as the sweeping action of the rotating strong magnetic field linked to the pulsar might suggest. This means that radiation seen to be coming from regions in the line of sight close to the pulsar originates only in the part of the surrounding shell outside this cavity, and it provides no direct information about the field close to the pulsar.

It is possible that the observations are consistent with the radiation of particles in the magnetic field produced by a toroidal current loop viewed nearly edge on. But it remains to be seen whether this model will survive more detailed observations. It is difficult to construct theories of the nature of the wisps of matter in the Crab because they provide such a radical departure from the average conditions around them, but their link with the glitches (sudden jumps in period) of the pulsar should help to provide a complete model eventually.

thus emerges as not quite the bogy it is often assumed to be, but a bogy nonetheless.

The really important source of SO_2 is domestic and industrial heating—that is, small localized sources related to the distribution of population and industry. Evidence for this comes from the variation of SO_2 concentration throughout the year. In cities concentrations are usually higher in winter than in summer in spite of the fact that emission from power plants is the same throughout the year or even higher in summer. Golden and Mongan thus suggest that as a matter of policy, where low sulphur-bearing fuels are available they should be directed to small emission sources in highly polluted areas rather than to the bigger power plants. In many areas of Britain, however, the situation may be a little different. In regions where the Clean Air Act has been applied the proportion of SO_2 at ground level attributable to small localized sources is probably smaller than in Illinois.

RADIO GALAXIES

Dichotomy Confirmed

by our Cosmology Correspondent

Optical spectra of nearby giant E and SO galaxies have been obtained by M. J. Disney and R. H. Cromwell at the Steward Observatory in Arizona. The spectrograms show a definite correlation between radio and optical activity in the galaxies (*Astrophys. J. Lett.*, **164**, L35; 1971). Earlier surveys of nearby galaxies have revealed that twenty-four of our near neighbours are radio sources. Most of these are fairly weak, but some are sufficiently strong that it has been suggested that they have quasars at their nuclei (Heeschen, *Astrophys. J. Lett.*, **6**, 49; 1970). These are known as active sources; the quieter, non-quasar-like radio galaxies are referred to as passive sources. This classification is far from being an arbitrary rule of thumb, because the active sources are all unresolved (radio diameters less than 1.5 arc sec) and the passive sources are extended over more than 1 arc minute, and show the "normal" inverse power law spectrum, indicating a thermal origin for the radiation.

The apparent similarity at radio wavelengths between some nearby galaxies and the general run of nearby quasars has been an attractive feature of these radio observations. However tenuous the link might be, many astronomers would be relieved to find a way to tie quasars into the normal evolutionary pattern of galaxies. Since Heeschen's work, these twenty-four nearby galaxies have been obvious candidates for optical study.

The latest survey, carried out on twelve of these radio galaxies, confirms this dichotomy. Disney and Comwell found that the spectral properties of these galaxies are related to their radio properties, but not in the way that might be expected on a naive quasar nucleus assumption.

Three of the galaxies studied by Disney and Cromwell have normal radio spectra, eight have the radio characteristics defined by Heeschen as active, and one seems to be an in-between case. All of the normal radio galaxies also show normal optical spectra. All but one of the active radio galaxies show emission lines of the type characteristic of planetary nebulae, and some of these lines are very strong. Although the sample of galaxies is rather small, the significance of this correlation is clearly unquestionable. Interestingly, the one active galaxy which does not show emission lines (NGC 4552) has already been shown to have an abnormally highly reddened centre, so that any emission lines originating in the nucleus might be obscured by matter around the centre of the galaxy (see, for example, Tifft, *Astr. J.*, **66**, 390; 1969).

In one of the spectrograms studied, that of the galaxy NGC 3998, the hydrogen alpha line is seen clearly, and has broad extended wings of the kind seen in the emission from quasars at this wavelength.

But unfortunately for the quasar nucleus model, the activity revealed by these spectrograms is not the kind normally associated with quasars. In general, quasars have strong, broad hydrogen lines, which are not seen in any of these nearby galaxies, except NGC 3998, and the excitation (measured by the relative intensity of 5007 [0111] to 3727 [011]) is much lower in these galaxies than in quasar or Seyfert galaxies and is more typical of planetary nebulae. Although it is now clear that Heeschen's classification really does define two separate families of galaxies, the processes differentiating between them remain obscure.

Explaining Away the Anomalous Background

Going by measurements at microwave wavelengths, the temperature of the universe is fairly certainly 2.7 K. This has been the consistent result since Penzias and Wilson in 1965 reported the detection of an isotropic background radiation at microwave wavelengths, apparently pervading the universe, which most likely is the fading glimmer of the flash that accompanied the start of the big-bang universe. But at wavelengths shorter than a few millimetres it is impossible to observe this radiation from the ground—the atmosphere is in the way. So do the surprisingly high fluxes that have recently been measured in the far infrared during rocket flights mean that something is wrong with the rocket experiments, or that the measurements at longer wavelengths cannot be extrapolated to the far infrared along the 2.7 K blackbody curve, or what?

The problem is important because the existence of the background radiation is the strongest card held by the proponents of the big-bang cosmology. It is extremely hard, for example, to account for the radiation as a result of the superposition of radiation from distant galaxies—it has to be that astronomers are recording something primaeval. But it would throw a spanner in the works if the radiation turned out not to follow the blackbody spectrum. Until there is an explanation of the anomalously high fluxes corresponding to 8 K which have been recorded in the far infrared on two occasions now, the big-bang cosmologists cannot be happy with their trump card.

The possible loophole is that the two rocket measurements covered a range of wavelengths, from 0.4 mm to 1.3 mm. Could it be that the radiation, in fact, follows the 2.7 K blackbody curve, but that superposed on the curve are spectral lines which lead to an average temperature of 8 K? There have been several hints that this could be so. There has been observational work which places upper limits on the temperature at a number of specific wavelengths in the 0.4–1.3 mm interval which are less than 8 K. One possibility that would fit is that there is a line between 0.8 and 1 mm. A report in next Monday's *Nature Physical Science* describes the results of such a search for lines in this interval and on either side.

Beery and his colleagues have been able to carry out their measurements from the ground by taking advantage of the low atmospheric noise at the Mauna Kea observatory, Hawaii. What they have done is to look for lines using the 24-inch telescope, and attempt to ascertain whether or not the lines are atmospheric in origin (by seeing whether the line strengths depend on the air mass observed by the telescope). They particularly draw attention to a line on the long wavelength side of 0.8 mm which conceivably has a bearing on the far infrared measurements. Most likely the line is attributable to N_2O, however. It seems to be atmospheric therefore, making it an awkward explanation of the rocket measurements, although it might account for recent balloon observations by Muehlner and Weiss (MIT) of an anomalously large far infrared flux.

It is probable then that the team working at Mauna Kea have drawn a blank. All the same theirs is a useful negative result—it is the first high resolution search from the ground for isotropic emission features in this spectral region, and it fixes valuable limits for explanations of the anomalous flux. But it looks as if the astrophysicists will have to look elsewhere for a solution.

NUCLEATION

That Factor 10^{17}

from our Molecular Physics Correspondent

THE strange controversy over the existence or non-existence of a factor 10^{17} in homogeneous nucleation rates seems to be dying down, leaving everybody not a little the wiser and more respectful of the subtleties of surface thermodynamics and the interplay of energy and entropy in very small systems. It is now nearly ten years since Lothe and Pound (*J. Chem. Phys.*, **36**, 2080; 1962) threw their carefully poised spanner into the works, arguing that the classical Becker–Döring–Volmer–Zeldovitch treatment of the dynamics of droplet formation contained a false prescription for the handling of translational and rotational degrees of freedom when notionally dispersing a bulk liquid into nuclei of almost atomic dimensions. The sheer size of the discrepancy introduced—about 10^{17} in steady-state concentrations, but logarithmically less in terms of critical supersaturation—indicated that something more than a poor approximation was to blame, though the issue was confused by other dubious factors such as the use of a "surface tension" to write the free energy of even the smallest nuclei. Lothe and Pound, with somewhat more courage of conviction than modesty, indicted the classical theory on the particular count that it failed to represent the considerable entropy due to the Brownian motion of clusters, both translational and rotational. They then applied what seemed to be the obvious correction for this, obtained the factor 10^{17} for typical cases and accepted quite cheerfully that it destroyed agreement with the, admittedly not impressive, experimental data on critical supersaturations available at the time.

Since then, argument has ranged back and forth in the pages of the *Journal of Chemical Physics* and elsewhere, at times seeming only to deepen the confusion, more recently shifting, it seems, decisively, in favour of the chief antagonists of the Lothe–Pound position, H. Reiss and J. L. Katz of UCLA. Now two important constructive reviews of the subject have appeared (H. Reiss, *J. Stat. Phys.*, **2**, 83; 1970, and P. P. Wegener and J-Y. Parlange, *Naturwissenschaften*, **57**, 525; 1970); the first makes a convincing attempt to say the last word on the translation–rotation paradox, the second reviews this in relation to more recent experimental results. The Wegener–Parlange article, incidentally, contains one of the best bibliographies in existence for this tortuous subject.

In this most recent critique Reiss meticulously reconstructs the basic equation for equilibrium concentrations of N-atom clusters in a supersaturated gas using a very general formulation in terms of the classical configuration integral and postponing all details of the geometry and internal mechanics of the clusters for as long as possible. The only assumption at this stage, apart from classical mechanics and gross spatial homogeneity, is the existence of geometrically distinct clusters in the condensing gas, corresponding to certain factorizations of the total configuration integral. Reiss then defines the physical clusters by a new collective property, introducing the idea of a minimum sphere enclosing all atoms present to replace the centre of mass used as the locating property in his previous treatments. This seems to be the crucial step in solving the problem, because use of the minimal sphere both allows the centre of mass of the cluster to fluctuate realistically and at the same time leads to a definition of clusters in a form as close as possible to the nature of an actual physical drop. When these assumptions are carried through—a process considerably more intricate than can be rendered here—the result is no longer a factor of 10^{17} but a relatively harmless coefficient or order unity which is later shown to arise quite naturally as a correction for the fact that real clusters are not isolated in their internal motions but exist subject to their own vapour pressure.

Although there are still passages in Reiss's argument where sleight of hand could cover a fallacy, the final result is convincing even without the accumulating weight of experimental evidence with which it now brings the whole theory altogether more into line. This evidence, much of it arising from supersonic nozzle experiments, is also reviewed by Wegener and Parlange (*loc. cit.*) and is added to in the form of critical supersaturation calculations in a recent article by J. L. Katz (*J. Stat. Phys.*, **2**, 137; 1970) using the Reiss approach. Readers of these columns will also have noted recent activity in the cause of molecular beam cluster studies which seem likely to yield much more direct information about the properties of small growth nuclei in the near future (see *Nature Physical Science*, **229**, 99; 1971).

Although the resolution of the "translation–rotation" paradox now seems to have gone against the original instigators, none of their critics has suggested that the flaw in Lothe and Pound's original argument was in any way superficial; on the contrary it is now generally recognized to have been embedded close to the heart of the central mystery—of how correctly to characterize a surface in micro-statistical terms while making a consistent guess (for it can still hardly be more) at the partition functions for the internal motions of small droplets. The considerable credit due to Lothe and Pound for throwing open the whole question is all the greater because, however dramatic the numerical factor involved, it was logical rather than numerical consistency which was at stake. At the same time Reiss and his collaborators can be well satisfied at having, so to speak, cleared the decks of a nasty theoretical problem in time for the next round of experiments.

Anomalous Water and Silicic Acid

ON page 31 of this issue of *Nature*, Barnes *et al.* clearly state their belief that the properties of anomalous water are no more than the sum of the properties of the impurities present and that anomalous water as such probably does not exist. Some support is given to this contention by the work of Adams *et al.*, an account of which appears in next Monday's *Nature Physical Science*; they claim that the "anomalous water" produced in their experiment is chiefly a silicic acid solution.

Adams and his colleagues have made use of the high surface to volume ratio of porous glass to create the same environment for the production of anomalous water as other workers who have used Pyrex capillaries, for example. They took a number of precautions to reduce contamination which included burning off organic impurities in the porous glass at 550° C in a stream of oxygen and the use of greaseless Teflon valves throughout the apparatus. They also used a quartz iodide lamp to irradiate the porous glass cell on the grounds that strong irradiation would enhance the surface reactions which have been generally thought necessary for the successful production of anomalous water. Adams *et al.* found that the liquid which condensed after passing through the walls of the porous glass container showed many of the properties of the anomalous water reported last year by Deryagin (*Sci. Amer.*, **223**, 52; 1970).

These properties are not spelt out by Adams *et al.*, but presumably they include high values for molecular weight and boiling point, for example. Desiccation of the liquid samples revealed solid bodies which contained between 10 and 30 per cent of silicon and about 5 per cent sodium by weight according to electron microprobe analysis. They point out that this is consistent with the work of Morariu *et al.* (*Nature*, **227**, 373; 1970), who found similar bodies in samples of anomalous water and conjectured that these solids had condensed from silicic acid solution; unfortunately, they performed no chemical analyses to support their hypothesis. Adams *et al.* suggest that the anomalous water which they produced is almost certainly a silicic acid solution and this goes a long way towards establishing experimentally that the chief characteristic of anomalous water may be that it does not exist.

Psychobiological Studies of Aggressive Behaviour

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Field studies of aggression in primates are only just beginning. Their fruits, however, could have considerable relevance to the human situation*.

ALTHOUGH there are obvious reasons for scientific interest in the evolutionary and developmental origins of human aggressive tendencies[1-4], there has been little work on this subject. For example, in the upsurge of primate field studies during the past decade, very few studies have paid primary attention to aggressive behaviour[5-9]. For this reason, Eric Hamburg and I have recently conducted an investigation of aggressive behaviour in chimpanzees and baboons in East Africa. For more than 200 hours we observed animals within ten yards of us, and with help from Jane van Lawick-Goodall in Tanzania and Phyllis Jay in Kenya, we collected considerable data on aggression in these two species.

By "aggressive behaviour" I mean actions in which an animal inflicts, or tries or threatens to inflict, damage on another animal—in other words, threat and attack patterns. I shall try to describe such patterns, to determine the conditions in which they occur, and the circumstances in which they are likely to be diminished or terminated, particularly by means of inter-animal communication.

We chose chimpanzees for our study because they are probably man's closest living relative. There are many similarities between man and chimpanzee in the number and form of chromosomes, in blood proteins, in immune responses, in DNA, in brain structure and behaviour[13]. The more we see of their behaviour, the more we are impressed with the resemblance between some of their communicative repertoire and that of the human species.

Goodall's research at the Gombe Stream Reserve in Tanzania[10-12] has the special assets of detailed, systematic, close range, longitudinal observation with full recognition of individual animals and their habituation to human observers. And her husband, Hugo van Lawick, has made an extensive film record of threat and attack patterns in chimpanzees, and the various contexts which elicit such patterns. He has filmed several types of threat behaviour, ranging from the low intensive threat (a slight tipping back of the head accompanied by a soft coughing sound) to high intensity threat (such as swaying back and forth in an upright position, or charging towards the animal which has elicited the aggressive behaviour). His films also show various attack patterns, ranging from a slap of the extended hand to a vigorous stamping on the back of the victim. Stones and sticks are used as simple but effective weapons[14]. Attacks are usually of short duration—on a time scale of seconds or minutes—and, immediately afterwards, the victim often approaches the aggressor with submissive gestures and is then apparently reassured with gestures such as an embrace or pat on the back. Indeed, Goodall has described a remarkable repertoire of submissive and reassurance behaviour patterns.

Goodall's observations and our own suggest that aggressive interactions are likely in connexion with (1) competition over food, especially if highly desirable foods are spatially concentrated or in short supply; (2) defence of an infant by its mother; (3) a contest over the dominance prerogatives of two individuals of similar social rank; (4) redirection of aggression (such as when a low ranking male has been attacked by a high ranking male and immediately turns to attack an individual subordinate to him); (5) a failure of one animal to comply with a signal given by the aggressor (for example, when one chimpanzee does not respond to another's invitation to groom); (6) strange appearance of another chimpanzee (such as a chimpanzee whose lower extremities became paralysed by poliomyelitis); (7) changes in dominance status, especially among males; (8) the formation of consort pairs at the peak of oestrus (this is quite a recent discovery among wild chimpanzees and requires further study).

Longitudinal study is essential to clarify the nature and extent of aggressive behaviour in the context of changes in dominance relations. These relations may be stable for long periods, but when they change, the level of violence is likely to increase. For example, van Lawick filmed a transition period in which a male first acquired a top ranking status. He was very aggressive, constantly threatening and often attacking his subordinates, but as months passed and his position apparently became more secure, he became increasingly tolerant of other chimps. During the several ensuing years, he has been the highest ranking chimp in this community, and is accorded much deference by the others.

Early Aggression

Goodall has also reported the development of aggressive patterns during the early years of life. For example, a ten month old male infant was filmed making typical threatening gestures, in a context similar to those of adult threat. These early aggressive patterns are much more characteristic of males than of females. Kinship is also important in the development of such behaviour; for example, a juvenile may threaten or attack chimpanzees older than itself if its mother is near and if her rank is higher than that of the victim. Adolescent males are often aggressive towards females when no higher ranking males are in the group, but apparently restrain such behaviour toward females when dominant males are present. As adolescent males mature, they tend to threaten the lowest ranking mature males and so gain admittance to the hierarchy of adult males. In general, adolescence is a turbulent, aggressive period among these chimpanzees.

Why study baboons? There are several reasons: (1) the adaptive success of the baboon-macaque group, having spread widely through Asia and Africa in various habitats; (2) the baboons are the largest monkeys; and (3) the relatively large extent of their ground-living capability, in a type of habitat (savannah) that was probably crucial in the emergence of early man.

Based chiefly on the extensive field work of Hall, Devore, Washburn, Altmann, Rowell, and Ransom, plus our own observations of baboons in two contrasting habitats, it is pos-

*This article is based on the first Sir Geoffrey Vickers lecture, given under the auspices of the Mental Health Research Fund in London in February 1970.

sible to summarize briefly the conditions in which baboon threat and attack patterns are likely to occur[15–21]. The species under consideration here is the common olive baboon of East Africa.

In certain circumstances the probability of overt threat behaviour and of fighting is higher than in the other contexts of baboon life. These include protection of the troop by adult males against predators such as lions and cheetahs; resolution of disputes within the troop by adult males; formation and maintenance of consort pairs at the peak of oestrus; attainment of preferred sleeping sites in the trees, particularly in the presence of predators; acquisition of premium foods such as figs, nuts, and bananas, especially when spatially concentrated rather than widely distributed (Figs. 1 and 2); dominance interactions, especially in the presence of premium foods, scarcity of sleeping sites, and females in full oestrus; exploration of strange or manifestly dangerous areas, a function largely of adult males; and contact between different troops, especially if such contact is infrequent.

Time for Aggression

Baboons, like chimpanzees, spend much of the day in peaceful activities, and there is abundant evidence of affectional systems, similar to those analysed by Harlow in rhesus macaque[22]. And so what circumstances precipitate aggressive behaviour? In trying to answer this question I shall deliberately discuss aggressive behaviour within the species and against other species.

The circumstances which I have mentioned as conducive to aggression in chimpanzees and baboons reveal that much of the behaviour occurs in two general categories: in defence and in obtaining access to valued resources. Within these general categories, various animals, objects or activities may be involved.

My list of situations eliciting threat–attack patterns in chimpanzees and baboons does not include the defence of a fixed territory; our observations are consistent with those of Crook[23]: "Comparative studies of forest fringe, and savannah *Cercopithecus* and *Macaca* monkeys, the baboons of the genera *Papio* and *Theropithecus*, the chimpanzee and gorilla do not provide evidence of rigorously defended territories".

Although most higher primates do not live in permanently fixed territories which they defend rigorously, there is a behavioural distinction between currently familiar and relatively unfamiliar territory. A savannah baboon troop may live in an area of 10–15 square miles for some weeks or months before moving to another nearby area. While it is living in a given area, the behaviour of its members tends to take on distinctive features at the fringes of this currently familiar space: they are highly vigilant, threaten readily, and some males move out a considerable distance beyond females and young in exploring the relatively unfamiliar area. An important topic for future research is the contact between groups in such circumstances. The limited data available suggest that there is considerable caution, vigilance, and agonistic behaviour when groups meet, although usually they seem to avoid serious fighting. In some conditions serious inter-group fighting does occur, for example, among rhesus macaque groups in cities in conditions of crowding, food shortage, and inter-species harassment[24].

Evolutionary Advantages

The observations of aggressive behaviour in higher primates deserve consideration in the framework of an adaptive evolutionary view of aggressive behaviour. Although we cannot be sure of the ways in which aggressive behaviour has functioned adaptively during the course of evolution, the following possibilities deserve serious consideration: (1) increasing the means of defence; (2) providing access to valued resources such as food, water and females in reproductive condition; (3) contributing to effective utilization of the habitat by distributing animals in relation to available resources—a spacing function of inter-group tension; (4) resolving serious disputes within the group; (5) providing a predictable social environment; (6) providing leadership for the group, particularly in dangerous circumstances; and (7) differential reproduction—it is compatible with present knowledge (though not proved) that relatively aggressive males are more likely to pass on their genes to subsequent generations than less aggressive males, because of the consort pairing at the peak of oestrus in which male aggressiveness plays some role.

Some of these factors may have given selective advantage to aggressive primates, if they could effectively regulate their aggressive behaviour. They have well defined cues that usually terminate aggressive sequences, and an elaborate repertoire of submissive behaviour. They have a stable and agreed dominance hierarchy that contributes to the predictability of the social environment, and they have clear, vivid sequences of aggression–submission–reassurance that have elements in common with the behaviour of man. Future research will profit from paying as much attention to the regulation and control of aggressive tendencies as to their sources and instigation.

If evolution is given serious consideration, it is difficult to overlook the likelihood that man has a vertebrate–mammalian–primate heritage predisposing him to aggressive behaviour. But what is known of the processes that govern the expression of such predispositions? To try to answer this question I shall consider the development of aggressive behaviour within the individual life cycle. Hormonal influences on brain organization early in life affect later aggressive and sexual behaviour[25–27]. Even brief treatment of newborn female rats with testosterone produces lifelong abolition of female sexual behaviour and a tendency to male patterns of aggressive behaviour. Pregnant rhesus macaques given large doses of testosterone during the second quarter of gestation produced female offspring which were abnormal[28] with some anatomical and behavioural characteristics of the male type. One of the well documented behavioural characteristics of this species is a sex difference

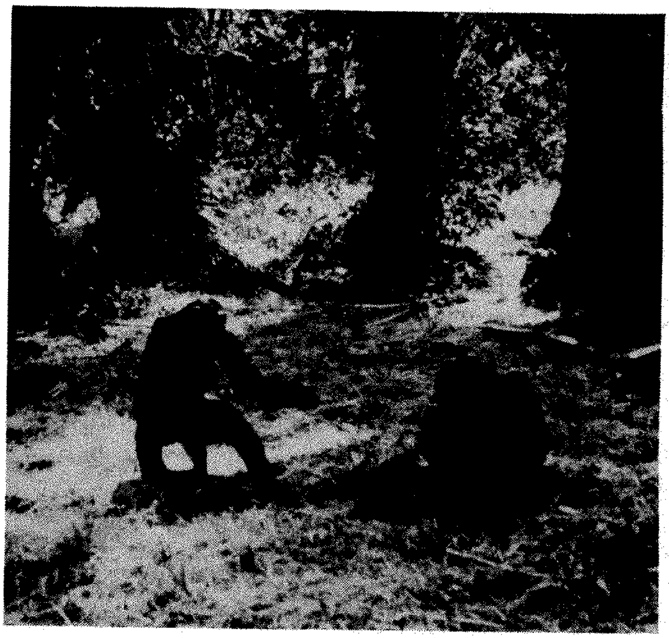

Fig. 1 An adult female chimpanzee approaches a highly dominant adult male which has been behaving aggressively in the presence of a premium food (bananas). She is reaching out in a manner which typically elicits a hug or pat; this is very similar to human patterns of greeting and reassurance. (Picture taken by Eric Hamburg.)

in the behaviour of infant monkeys, the males being more aggressive. This difference can be measured reliably in the first few months of life in the laboratory. Similar sex differences in aggressive behaviour have been observed in wild macaques and baboons.

Female infants of mothers given testosterone during pregnancy are more aggressive than normal females. They threaten other infant monkeys more often, initiate play more often, and engage in rough and tumble play more often than do normal females.

During growth and development, many influences can modify the expression of these aggressive patterns. For example, undue infant aggressiveness may be severely punished by larger and more powerful animals, leading to fearful inhibition later in life. In view of these possibilities for environmental influences during development, it is interesting that there is some tendency toward persistence of hyper-aggressive characteristics into adult life in females whose mothers are exposed to testosterone in pregnancy.

Human Development

Is there any evidence that testosterone has similar effects on the development of behaviour in humans? We have been able to study a few cases of girls who had been exposed to androgens *in utero*. At the Pediatric Endocrine Clinic at Johns Hopkins University, John Money has been conducting a long term programme of research, and a report has been published on twenty-two girls, mostly studied in late childhood and early adolescence[29]. Those with striking anatomical abnormalities had undergone surgical treatment shortly after birth. By means of interviews and projective tests, information was obtained from each girl and from at least one parent in each of several behavioural categories. The research design undertook to control for observer bias. Results indicated that the early androgenized girls, in contrast with a control group, tended to be described by themselves and others as tomboys, to engage in outdoor sports requiring much energy and vigour, to prefer rough play, and to prefer toys ordinarily chosen by boys (such as guns). This initial study requires replication, even though replication will necessarily be difficult. This line of inquiry has led from basic research on the biology of sex differentiation to an important human problem. The results are at least compatible with the concept that testosterone is one of many influences which shape the development of aggressive behaviour in the human species[30].

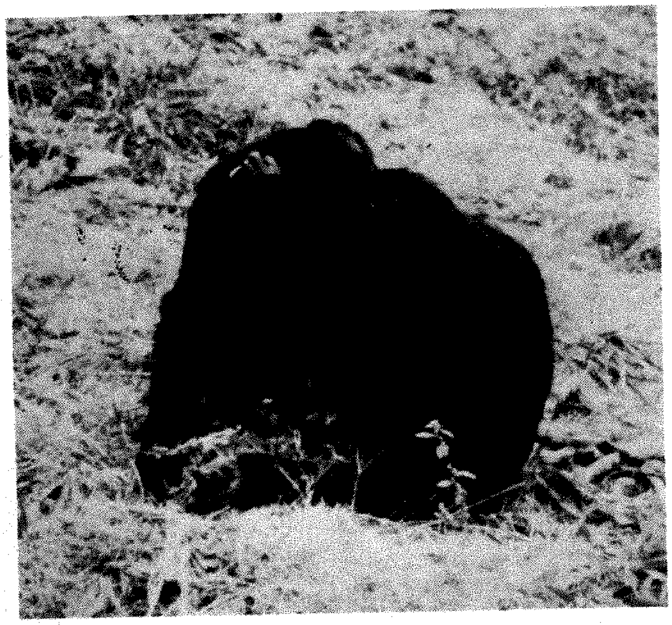

Fig. 2 Two adult male chimpanzees engaged in an intense, prolonged session of mutual grooming, immediately after aggressive interactions over premium food (bananas). (Picture taken by Eric Hamburg.)

Does the exposure of foetal brain to testosterone have a distinctive influence on the differentiation of circuits that will later mediate aggressive responses? This seems likely in the light of current research on biochemical mechanisms of brain differentiation[31]. This does not, however, suggest that testosterone establishes fixed patterns of complex behaviour, unmodifiable by subsequent events. More likely, the hormone affects the brain in such a way as to facilitate the learning of aggressive patterns later in life. For any species, some patterns of behaviour are easy to learn, some fairly difficult, and some exceedingly difficult[32]. In general, patterns that have been valuable in species survival are easy to learn[33]; and hormonal influences on brain development may have important mediating roles, especially where sex differentiation is concerned[34]. One way this can occur is through differences in the development of attention, for attention is crucial in learning processes. A hormonal influence during a sensitive period of brain development may render a certain class of stimuli more interesting to the organism at a later stage. This line of inquiry is amenable to experimental analysis in primates.

Visual Stimuli

Do some types of visual input elicit more sustained attention from infant monkeys than others? In one experiment, monkeys were raised in a total isolation chamber for the first nine months of life, during which they were exposed to various types of visual input from coloured slides[35]. These slides depicted monkeys in various activities and also depicted various non-monkey stimuli. Monkey pictures elicited much more interest than non-monkey pictures, and moreover, pictures of monkeys showing a species-typical threat expression were especially potent in eliciting behavioural responses. Between two and a half and four months of age, threat pictures yielded a particularly high frequency of disturbance. Similar results were obtained with films in the same experimental design (personal communication from G. P. Sackett). As with most studies in this new area of scientific inquiry, this calls for replication. It suggests that the infant rhesus has a built-in, special responsiveness to the threatening facial expression which is characteristic of its species. Given a responsiveness of this sort, it is not difficult to imagine how the infant in the natural environment would learn a great deal about threat and attack behaviour. Once the infant monkey's attention was powerfully drawn to threat stimuli, he would rapidly learn the conditions in which threat and attack patterns were likely to occur, and the actions likely to terminate aggressive sequences.

This brings me to a consideration of observational learning in primate adaptation[36]. Traditionally, discussions of aggressive behaviour have associated unlearned responses with non-human creatures and learned responses with humans. Curiously, this linkage has persisted in spite of the enormous research literature on learning in non-human animals.

One of the most interesting findings of the primate field studies in the past decade has been the recurring theme of observational learning in a social context[37]. In many species and diverse habitats, the following sequence has been described: close observation of one animal by another; imitation by the observing animal of the behaviour of the observed animal; practice of the observed behaviour, often for some hours after its occurrence, especially in the play group of young animals. This sequence of observation, imitation, and practice has been described in relation to several adaptive situations: food gathering, tool-using and tool-making (in chimpanzees), nest building, infant care, copulation and aggressive interactions. In essence, the

R363

young have access to virtually the full range of adult behaviour, and take advantage of it to learn patterns of behaviour that have been effective in adaptation. The motivation for such observational learning seems to be well established in the young primate. Observational learning in monkeys has also been studied experimentally. It has been demonstrated that one monkey readily learns from watching another in food choice situations. Moreover, the observing animal learns from incorrect as well as correct responses of the animal he is watching[38]. In other words, he learns from the consequences of the operating animal's behaviour.

Sex Differences

In this context, our field observations are consistent with two concepts: (1) aggressive patterns are learned early in life through observation–imitation–practice sequences; (2) there is a sex difference in the attractiveness of some aggressive patterns from infancy onward. In baboons and chimpanzees, aggressive play is prominent during growth and development, with males spending considerably more time than females in such activities. Chimpanzee males (and also gorillas) make elaborate aggressive displays in adult life, and the young males, even in infancy, show more interest in such behaviour than do females. Young males are keen observers of older males in such matters.

This line of inquiry is important for an understanding of the influence of the social environment on the development of aggressive behaviour. It provides another link between evolutionary and developmental views of the organism. Lately, developmental psychologists have been calling attention to the importance of observational learning in young children[39]. The child between one and two years of age is a devoted watcher. At this age, observation and imitation may well provide his principal mode of learning.

A remarkable set of findings has highlighted the susceptibility of children to learn aggressive patterns by viewing models which act aggressively. For example, in one experiment pre-school children were exposed to an aggressive model attacking a target object for ten minutes in a laboratory situation, while a control group experienced the same situation without an aggressive model. When the children were tested in the same situation six months later, the former were much more aggressive towards the target object than the latter—that is, a ten-minute exposure enhanced physical aggressiveness in the same situation six months later. This experiment is one of a series carried out by Bandura and his colleagues at Stanford during the past few years[40,41], showing vividly how children can learn aggressive patterns by watching film or television and enact these patterns in their later play. He has shown that pre-school, middle class children tend to imitate the aggressive behaviour of adults whether they observe it in people in their presence or depicted on film; moreover, the effect is obtained even with cartoon films. In short, aggressive patterns are imitated whether the dramatic presentation is realistic or fantasy-like. Imitation is increased if the aggressive model is rewarded in the drama, decreased if the aggressive model is punished. In general, these imitative acts are displayed spontaneously in the play of these young children, sometimes in remarkable fidelity to the model's original behaviour. But recent work goes beyond this, showing that the children are capable of performing imitatively many more aggressive acts than they show spontaneously—provided they are given an incentive for doing so. Thus, there is a tendency to restrain expression of aggressive patterns in spontaneous play; this is particularly true for girls and for patterns in which the model has been punished. But the patterns have been learned, and their performance can readily be elicited by a suitable incentive. It is worth emphasizing that these studies rely on direct observation of the child's behaviour in the experimental setting.

Thus, it seems that biological predispositions to learning aggressive patterns and exposure to specific social learning situations may interact to produce great individual differences in aggressiveness during later life[42,43]. In analysing such problems scientifically, the effective conjunction of biological and psychosocial disciplines—so far rarely achieved—holds much promise for future understanding. It hardly seems necessary to point out the aggressive tendencies of the human species today. Whatever adaptive functions such behaviour may have served in man's evolutionary past, there is serious question about its utility in contemporary society[44]. The risks inherent in such behaviour have been greatly amplified within our lifetime. Yet these problems at present attract only a modest amount of attention in the scientific community. It is difficult to imagine a more important area for research in the future.

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Role of the Research Councils

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Last December a working party was set up by the Council for Scientific Policy to review the role and function of the research councils in Britain. At the invitation of the Editor of *Nature*, the secretary of the Medical Research Council has defined the problems facing the councils, and drawn some personal conclusions about future needs.

BRITAIN invests considerable sums in research, and of this rather more than £100 million are spent through the research councils. Most people would agree that in spite of the importance of the educational and cultural aspects of scientific knowledge, sums of this order are provided because the nation expects a practical return for its investment, at least in the long term. The question that is being asked is: what sort of organization of this area of science is likely to provide the best return for money? This objective has to be considered in the light of the nature of science. Science stems from original ideas; original ideas are the products of independent minds and, by definition, nobody can order originality or predict its outcome. This is important but it must not be forgotten that there is much hard and often tedious work to be done as well.

The aim therefore is to use science, with full regard to its nature, to achieve the practical ends which Britain requires. To do this, the administration must carry out certain tasks. These can be summarized, though inevitably with oversimplification. If research is to be done there must be a national capacity to do it and, unless the future is to be mortgaged, an important task is to maintain and develop that capacity; this is a capital investment. This task demands, for example, the formulation of postgraduate training award policies, the support of particular disciplines, the encouragement of interactions between fields and the maintenance of a broad foundation on which the at present unforeseen needs and opportunities of the future can build. The next task is to define objectives. Usually in research there is no straight course to the mark, and most of the course is likely to be unknown at the start; this does not, however, make it any the less important to know where the mark is. The determination of the broad objectives and priorities is clearly a matter in which the government has a considerable interest. The problem is largely one of relating, on the one hand, estimates of the benefits hoped for and, on the other, estimates of the chances of success, likely time scale, etc., in the existing state of knowledge. A further task is to formulate and execute the policies needed to achieve the objectives with regard to the nature of science. The final task I wish to mention is that of communicating results of practical importance to users and providing advice on the interpretation of results.

Interrelations of Science

The concepts of the scientific capacity of the country and its development, and the formulation of scientific policies with objectives in view, relate to what are sometimes called the "horizontal" and "vertical" elements in the structure of science.

The horizontal elements relate to the development of a coherent body of knowledge within disciplines or schools of thought. Individuals, universities and learned societies are basically responsible for these. Nonetheless, the research councils have a significant role to play, perhaps particularly in relation to the balance between disciplines, through their support of university research and training complemented by the use of their own establishments. It is the research councils collectively which are responsible for the provision from public funds of selective support for science in the universities. The policies of the councils, which need to be and increasingly are being coordinated, can play a significant role in the pattern of research. The councils can encourage particular disciplines; some, for example dentistry or nuclear physics, are within the responsibility of a single council; others, such as psychology or biochemistry, need coordinated action from more than one council. The need for horizontal integration is widely accepted and the research councils are very conscious of their joint responsibilities for coordination.

The vertical element in the structure—the development of knowledge towards practical objectives—is the one which appears to be the more controversial. Thus one type of solution put forward to solve these problems of organization is to divide research into "pure" and "applied", and to separate them administratively. Funds for pure research would then have to be justified as a whole but in isolation from the impact of its practical application; they might be justified as support for higher education. This is obviously a possible line of argument and I think it important to discuss the distinctions between pure and applied research, particularly in relation to medical research, and to ask whether a useful division is possible. In the medical field most people think of clinical research as the applied end. To a great extent this is true, but much clinical research is long term in its aims and fundamental in its results. Equally, much laboratory work in medical research is short term and has immediate practical implications. Clinical research is normally carried out by individuals with small teams and it is carried out particularly in teaching hospitals in universities. The same is true of laboratory research in the medical field; the great exception is, of course, the major and important work of industry, particularly in therapeutic substances. Organization in small teams is also found in the so called applied parts of fields other than medical research. It applies equally to much work in chemistry and in engineering and agricultural faculties in universities, to much of the work of the Science Research Council (SRC), and to much done in institutes of the Agricultural Research Council (ARC). Research teams in many fields may undertake some projects of a long term nature and others intended to solve short term problems. It is sometimes only when the results are obtained that it is possible to say whether a project is long term or short term in its implications.

There are, of course, areas of research, for example aircraft, which because of their special demands must be treated separately. However, scientific policies designed to advance knowledge towards general answers to particular practical objectives must include training and research developments over the whole range of relevant studies, pure and applied. Such policies will clearly be most effectively formulated and executed by a single body when this is practicable. Furthermore, since any particular scientific project has its place on both horizontal and vertical dimensions, the two cannot logically be separated. The fitting of general answers to situations particular in respect of place, time or political need is by its nature a separate problem.

Medical Research Council

I would like now to describe something of the role and operation of the Medical Research Council with a view to illustrating some of these points. The council's purpose is to advance knowledge which will improve the health and capability, both physical and mental, of individual members of the population; this involves not only the prevention of disease and, should prevention fail, its treatment, but also a positive approach to improving physical and mental wellbeing. Such knowledge is of value not only to medical men but to many others including, for example, planners, educationists, social workers and industrialists; it is of value to the various health departments and to many other activities of government. The research is carried out whenever possible through the agency of a university but this is complemented by the direct employment of staff. In order to achieve results, to play its part in developing Britain's scientific capacity and to make the best use of individual originality, the council has three broad policies. These are: to support in its particular field work which is of outstanding quality regardless of subject; to provide at least a minimum of support over this whole area of science, and to support and undertake research in accordance with scientific policies designed to encourage a balanced development of knowledge from fundamental research towards practical objectives, particularly in priority fields. (For further information on council policies see MRC annual reports for 1968–69, 1969–70 and 1970–71, yet to be published.)

The council keeps the whole of its field under review and decides at regular intervals which areas, organized towards broad practical objectives, should be reviewed in greater depth or given priority. It also determines reviews and priorities in relation to disciplines which need special encouragement. In determining priorities and areas for review the council hears the views of the health departments, whose assessors attend council meetings, of users, since the clinical members of the council are all practising members of the medical profession as well as investigators, and of other government departments and users through various committees. In general, the statement of objectives is not contentious; we all know we want to prevent or cure cancer or heart disease or mental disorder. The problem is not to state the objective but to find the means to reach it. To formulate policies to work towards such objectives, all approaches must be taken into account. This can be illustrated by examples.

Recently, the council published a report on radiobiology, which deals with radiation hazards and radiotherapy (MRC annual report 1968–69, page 11), and on biochemical research in psychiatry[1]. Summaries of other reports, three on drug dependence and one on applied physiology, will be published shortly. Each illustrates the essential need to include a broad range of scientific coverage in such studies. The radiobiology report advises, among other things, that the most practical approach to the immediate applied problem of the quantification of risks from levels of radiation near normal background "should increasingly proceed by analytical methods defining the process of damage and recovery", that is, at sub-cellular levels. This field is one of long standing collaboration between the ARC, which is responsible for food, and the MRC; there is a joint standing committee on monitoring fall-out. The reports on drug dependence range from the chemistry involved in tracing breakdown products, through pharmacology to social problems. The Social Science Research Council (SSRC) is represented on the joint working party set up to implement the recommendations. Applied physiology, a partner to applied psychology on which there was a report a few years ago, is concerned with man in his environment and his efficiency at work. This field is one which used to be under the aegis of a joint MRC/DSIR (Department of Scientific and Industrial Research) board and at present requires consultation with both SRC and SSRC. A joint report will soon be published on the work of all five councils concerned with pollution. The MRC has also recently undertaken studies of certain disciplines, in particular, clinical pharmacology, obstetrics and gynaecology, mycology and dermatology.

The report on biochemical research in psychiatry[1] is a useful example to illustrate in a little more detail how the council can operate towards a specific objective. As is well known, this is an extremely difficult field of research. In spite of the large growth in knowledge of the mechanisms and behaviour of nervous systems, it is still very inadequate. Furthermore, the technical problems of relating the available knowledge of the nervous system with changes which occur in mental disorder in the intact human are immense. Of particular importance is the fact that there is a great shortage of people with the appropriate training and interests. Simply supporting psychiatrists to make observations on sick patients in mental hospitals will not solve the problem. There is clinical research to be done, but the committee recommends more work of a fundamental nature and in particular more work in what it describes as "bridging disciplines". It also notes the shortage of psychiatrists who have sufficient training in methods of investigation. The council has accepted the recommendations and is acting on them. It can support work in which there is interest and activity by awarding grants in response to applications; this applies in various fields of neurobiology. Sometimes an active initiative or special facilities are required. The council is tackling the bridging area by re-forming an old establishment and constituting a new one, each with both clinical and various laboratory studies. The MRC can also attempt to improve the shortage of trained personnel. It can give training awards and fellowships, make staff appointments and give grant aid for assistantships; more important, it can, with its long term programme grants and groups, help to strengthen the research sides of departments of psychiatry. The moral of this example, and it is typical of many, is that the best approach involves a combination of varying aspects of laboratory and clinical research, together with a need to encourage a discipline and to increase training.

This example raises other relevant issues. In the formulation of the policy, in its implementation and in the staffing of the multidisciplinary establishments, the council has to be deeply involved in many aspects of fundamental neurobiology. However, for good reason the SRC is also interested in neurobiology; the two councils therefore have a joint committee on the subject. The neurobiological approach to mental health considered in this particular report is only one; there is also a great range of very important problems on the interface of psychiatry and sociology, and in research units concerned with social aspects of psychiatry the MRC has received help from the SSRC.

There are a number of disciplines which have to be an integral part of the work of more than one council if each is to fulfil its responsibilities; biochemistry, physiology and psychology are examples each involving three or four councils. There are also areas in which more than one council may be involved in policies designed to advance knowledge towards a broad practical objective. Specific examples have already been mentioned; more general examples can be given. The MRC has sections dealing with social medicine and environmental medicine which must have close connexions with respectively the SSRC and the Natural Environment Research Council (NERC). The MRC is concerned with nutrition, the ARC with food; there is a joint committee covering both fields. There does need to be very close coordination between councils; it has been improved considerably and is being further developed.

The principal user, in a practical sense, of the knowledge covered by the MRC is the medical profession; communication with the medical profession is largely through scientific publications, scientific meetings and so on. The council has, of course, close relations with the various health departments. There are important aspects of these relationships which have no bearing on information and advice, and I shall not consider them here. Close liaison is maintained by mutual representation on committees, through officers and by formal communication. The same is true of a number of other government departments, and since these relationships are less obvious I will give some examples. The council advises the Overseas Development Administration of the Foreign Office and the funds for tropical medicine of ODA and MRC are distributed on advice from a board of the council. Similarly, work for the Army and Navy is dealt with by standing joint committees. Problems ranging from food additives to the trawler disasters have been investigated for the Ministry of Agriculture, Fisheries and Food, sometimes by joint committees. There has been constant communication with various departments on industrial conditions, environmental problems and so on, and with the Home Office on subjects such as drug dependence and delinquency.

Another general and important point arises out of the previous paragraph. The research councils have an advisory function, often to government but sometimes to other public bodies, and it can be of advantage to government, parliament and the public to be able to get a scientific view from a body which is not only independent but can be seen to be independent of the department responsible for the decision. Probably the major examples of this in the past have been the Medical Research Council's advice on problems of radiation and safety.

Some Conclusions

I should like now to make some conclusions which are essentially personal. I have suggested that administration in the areas of science under consideration is concerned with four broad tasks: the development of the scientific capacity of the country, the definition of objectives, the formulation and execution of scientific policy and the communication of results and advice. Of these the first and third are matters of administration of science; the other two involve not only science but other areas of national life.

I think that there would be little disagreement that the two scientific tasks taken on their own would be best served by keeping the administration of the main core of pure and applied science as closely coordinated, and indeed integrated, as practicable. The attainment of practical ends could only be hindered if scientific policies could be neither formulated nor implemented effectively. As has been illustrated, such policies need to cover not only a wide range of research, both pure and applied, but also questions involving the development of disciplines. The practical need in administering these tasks is for a flexible structure which will enable the horizontal and vertical—and any other—dimensions, used to describe the pattern of science, to be considered together, and which can change with changing patterns of science and social and economic need.

The task of communicating results and advice in a way which will achieve changes in practice needs thought. It involves several elements. There is communication by means of journals, meetings and scientific or professional bodies; this is, or can be, an effective means in relation to medical practitioners, engineers, industrial scientists and so on. There is communication with government departments; to achieve this there is and must be a considerable network of committees and personal contacts because results in any particular area of science may have impacts in many parts of government. The most difficult task is probably to get information, in suitable form, to others such as farmers, small firms which do not employ professionals and even, sometimes, large firms in science-based industry in relation to less familiar problems, such as human factors in engineering design. Whether or not systems of communication, such as the existing advisory services of MAFF, should be set up and by whom they should be run are essentially political questions; scientists and administrators of science can only express a willingness to help.

The question of how to distribute finance and to determine priorities is undoubtedly crucial. This is a matter in which government departments, usually several in respect of any one council, have a genuine interest. Objectives are often easy to name and may in any case be first noted on the research side. It is usually more difficult to assess the feasibility and the effect that a particular use of research capacity will have on the progress of other research; these are matters of scientific judgment. The value of achieving the objective should be balanced against feasibility and the likely cost to other lines of work. All councils have day to day machinery for dealing with such matters; for example, assessors from departments sit on councils, officers are in constant contact at all levels and there are many joint committees. There may be a need to improve such machinery and there may be times when it does not function adequately and major differences remain unresolved. The final judgment and sanction do and must lie with government; it is for government to determine by whom the judgment should be made between the conflicting interests of professional and industrial users, of different government departments and of the general development of the country's scientific capacity.

There are problems which need consideration: how to improve coordination in the administration of science; how to improve communication with users; how to improve the responsiveness of science to national needs. When these problems are discussed one thing must be remembered: the hard task is not in recognizing a need or in communicating an answer, it is in finding the answer to meet the need.

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Antimatter in the Universe

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The models of nucleosynthesis discussed in this article could give clues to the possible existence of aggregations of antimatter in the universe.

THE symmetry between the properties of particles and antiparticles has been established with great accuracy. In particular, it has been shown from quantum electrodynamics that the electromagnetic interactions responsible for atomic properties are the same for matter and antimatter, so that it is impossible to distinguish these two forms of substance by optical measurements. It is very natural, therefore, to ask whether our universe is made only of matter or by both matter and antimatter.

From the point of view of astrophysics, two basic questions have to be answered if the latter possibility is to be considered seriously. The first is commonly stated as "Where does antimatter come from?" It is a difficult question because it obviously amounts to asking for a theory of the origin of matter itself. On the other hand, there is very good evidence, particularly from γ-ray observations[1], that at least the larger part of our galaxy is made chiefly of ordinary matter. The second question is therefore: "How can matter and antimatter be organized in units as big as a galaxy?"

According to the conventional hot big-bang model of the universe there was a small excess (~ 1 in 10^9) of baryons over antibaryons in the early stages of evolution, when the thermal energy kT exceeded the rest energy m_pc^2 of a baryon. It is to this excess that we owe the present existence of matter in the universe, for as the thermal energy dropped below mc^2 the baryons and antibaryons annihilated one another, leaving just the excess baryons intact. It has occurred to many people that it would be attractive to do away with the small excess of baryons at the early stages, if only a method could be found for separating matter from antimatter on a suitable scale before the annihilation set in. (Extensive references are given in the papers of Steigman[1] and Harrison[2].)

So far no satisfactory separation mechanism has been discovered. In view of the importance of the question, however, I believe that strenuous efforts should be made to find such a mechanism or to prove conclusively that none is possible. My aim in this article is to draw attention to a new possibility for a separation mechanism and to discuss some of its implications. The mechanism is based on the possibility that the thermodynamic properties of thermal radiation can be significantly modified by strong interactions[3-5]. It is an open question whether the Gibbs potential Ω for radiation, which is defined by

$$e^{-\Omega/kT} = \text{Trace } e^{-H/kT} \qquad (1)$$

(where H is the total Hamiltonian including strong interactions), has no singularity as a function of kT for large values of the temperature (see, for example, ref. 6). Such a singularity might be the indication of a phase transition. To be more specific, it is important to see whether there is some aspect of the strong interaction which gives an indication that such a phase transition exists and that its effect is to separate spatially nucleons from antinucleons.

One such model has been analysed in some detail. It starts from results of the mesonic theory of nuclear forces arising from the exchange of mesons between nucleons. The modern approach to this theory is to use dispersion relation techniques. From a fit of nucleon–nucleon scattering by the exchange of π, η, ω and ρ mesons, the nucleon–antinucleon scattering amplitude can be derived. There are bound states of nucleon–antinucleon pairs which can be identified with the mesons π, ρ, ω, η[7]. Such a situation in which the same particles appear as bound states (or resonances) and as agents for the forces is a special case of the notion of "bootstrap" for particles.

Current theories of particles place on the same footing elementary particles and bound states, which should be taken into account when dealing with the thermodynamic properties of a system containing nucleons and antinucleons. An adequate formulation for the foundations of statistical mechanics has been proposed[8] which can be summarized in a basic formula relating the Gibbs potential Ω to its value Ω_0 for free particles (including bound states) and to the collision matrix S

$$\Omega = \Omega_0 - \frac{kT}{2\pi_i} \int dE\, e^{-E/kT} \frac{\partial}{\partial E} \text{Trace}\, [(\text{Log}\, S(E))_c e^{-\Sigma \mu_i N_i}] \qquad (2)$$

E is the total energy parameter, and the index "c" means that only connected terms in the sense of quantum statistical mechanics should be taken into account. The values of N_i are additively conserved quantities (charge, baryonic number . . .) and the values of μ_i are the corresponding chemical potentials. A special case of formula (2) is the classical Beth–Uhlenbeck expression for the second virial coefficient b_2 of a gas in terms of the scattering phase shifts $\delta_l(E)$ describing the collisions between two particles of the gas

$$b_2 \simeq \frac{1}{\pi} \sum_l (2l+1) \int_0^\infty \frac{d\delta_l(E)}{dE} e^{-E/kT} dE \qquad (3)$$

No term associated with bound states is written in equation (3) because, according to formula (2), it is already included in Ω_0. The detailed justification of this point is an important feature of the Dashen–Ma–Bernstein approach.

Formula (3) shows the root of the effect of separation between nucleons and antinucleons: when bound states exist, some phase shifts in $N-\bar{N}$ scattering start from the value π at the threshold energy for collisions and go down to zero when the energy becomes large. This property is known

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as the Levinson theorem and is valid in the calculations of ref. 6. As a result, b_2 can be negative, just as it is for a repulsive interaction (which I shall call a statistical repulsion), although the nucleon–antinucleon interaction is chiefly attractive. (Similar effects are known in the theory of dissociation.)

Formula (2) is very convenient when dealing with elementary particles where the scattering amplitudes (the S-matrix) are known from experiment or from theoretical models whereas the Hamiltonian H is neither known nor useful. Using (2), one can investigate the behaviour of Ω as a function of the densities N and $\bar{N}$ of nucleons and antinucleons in thermal radiation. It turns out that the statistical repulsion is larger than any repulsion in the ordinary nuclear forces. On the other hand, one must take into account the effect of annihilation, which can be done by using a version of the Fermi statistical model. The result of the analysis is that, using conventional data, one finds a phase transition at a temperature kT of the order of 350 MeV. Above that temperature, nucleons and antinucleons tend to separate spatially from each other as a result of their statistical repulsion, so that the equilibrium local density of baryons $B=N-\bar{N}$ is found to be a non-zero quantity $\pm B_0(T)$, vanishing at the critical temperature. To be sure, it should be stressed that knowledge of strong interactions is too incomplete to prove that such a phase transition actually exists, but the analysis could be made more reliable by better data about nucleon–antinucleon scattering. I shall consider the existence of a phase transition of a type with an appropriate critical temperature as an Ansatz when I describe the evolution of matter in a big-bang model of the universe. Much of what I shall say would be valid in some other types of cosmologies, such as a version of Missner's mixmatter universe where previously independent systems of matter and antimatter come into contact.

Consider the simplest model of a universe which is initially filled up only with thermal radiation. Its expansion is described by a scale factor $R(t)$ which behaves approximately like $t^{-1/2}$ while the temperature varies practically like R^{-1}. For the early stages of the universe the effects of space curvature are negligible. It is known that the history of such a model can be divided into several periods, according to the content of thermal radiation: the hadronic ($kT \gtrsim 100$ MeV), leptonic ($kT \gtrsim 1$ MeV) and radiative ($kT > 3{,}000$ K) periods. Superimposed on that division, the evolution of baryons will lead us to consider three other periods: the separation ($kT > 350$ MeV), annihilation ($kT > 25$ KeV) and coalescence ($T > 3{,}000$ K) periods.

In the separation period, nucleons and antinucleons separate spatially as a consequence of their statistical repulsion. This is initially induced by fluctuations and one can compute the size d that individual condensations containing an excess of nucleons or antinucleons reach during the 10^{-5} s of that period. It is essentially controlled by diffusion so that $d \simeq (Dt)^{1/2}$. Taking for the diffusion coefficient $D \simeq c \times 1$ fermi and $t=10^{-5}$ s gives $d \simeq 3\times10^{-4}$ cm. Since the baryonic density B is then of the order of the nuclear density, the total baryonic number of such a condensation is typically 10^{28}. Near the end of the separation, the universe is filled with an emulsion of nucleons and antinucleons with a typical size d.

Next comes the annihilation period. When T falls below the critical temperature, nucleons and antinucleons tend to annihilate. Disregarding secondary effects for the sake of brevity, the annihilation process is found to be controlled by diffusion so that the densities N and $\bar{N}$ of nucleons and antinucleons satisfy the equations:

$$\frac{\partial N}{\partial t} = D\nabla^2 N - \alpha N\bar{N}$$

$$\frac{\partial \bar{N}}{\partial t} = D\nabla^2 \bar{N} - \alpha N\bar{N} \tag{4}$$

and for the baryonic density $B=N-\bar{N}$

$$\frac{\partial B}{\partial t} = D\nabla^2 B \tag{5}$$

From equation (5) one derives the evolution of the correlation function for B

$$< B(0,t),\ B(x,t)> = [4\pi D(t-t_0)]^{-3/2} \int < B(0,t_0)\ B(y,t_0)> \exp\left\{-\frac{(x-y)^2}{2D(t-t_0)}\right\} \mathrm{d}^3 y \tag{6}$$

As a result, the size of the fluctuations remains equal to $\sqrt{Dt}$ and the average baryonic density at time t: $(< B^2(0,t) >)^{1/2}$ is of the order of the fluctuation $(\Delta B^2(t_0))^{1/2}$ at time t_0 (10^{-5} s), within a region of size $(D(t)t)^{1/2}$, times a factor $(t/t_0)^{-3/2}$ coming from expansion. In practice, expansion leads also to the replacement of Dt by $\int D(t)\,\mathrm{d}t$. When computing $(\Delta B^2)^{1/2}$, one should take into account the correlations induced into the system by its originating from an initially homogeneous radiation. At the end of this period a typical fraction 10^{-8} or more of the initial nucleons survives. They are still in the form of an emulsion with a typical size 10^5 cm, and a typical mass 10^{10} g, within a sphere of this radius. This is very far from a galactic mass and it is essential in this theory to find a mechanism which could lead to the coalescence of matter and antimatter into larger units.

During the coalescence period annihilation gives birth chiefly to pions and, through their decay, to high-energy photons, electrons, positrons and neutrinos. The transfer of momentum by the photons and electrons produces an annihilation pressure at the boundary between matter and antimatter. (The existence of this annihilation pressure was pointed out by H. Alfvén and O. Klein[9].) This pressure is exerted over a distance $\lambda\gamma$, the mean free path of high energy photons.

To find the behaviour of matter and antimatter which are in contact along a common boundary is a rather complicated problem in fluid mechanics. The effect of high energy photons (and leptons) is a dominant feature because these particles exert a very strong pressure and keep heating the system. Radiative pressure is dominant, so that the pressure due to heating tends to balance the annihilation pressure. It has been shown that, at least for two-dimensional configurations, only the linear and circular boundaries are stable and that other shapes of boundaries suffer deformations which tend to increase their radius of curvature, as long as it is smaller than $\lambda\gamma$. The actual problem in cosmology is also difficult for geometrical reasons. Matter and antimatter are distributed in an emulsion and their boundary is most probably a very complicated Gordan surface. It can be shown, however, that if there is a systematic excess of photons entering one side, such as would be produced by a bulging of the boundary, there should be a rapid compensating motion of the boundary. This suggests very strongly that the annihilation pressure tends to keep the size d of the emulsion to the order of $\lambda\gamma$ when $\lambda\gamma$ increases by expansion. Irreversible thermodynamics also leads to the same conclusion.

During the annihilation period, $d \gg \lambda\gamma$. The equality $d=\lambda\gamma$ takes place for $kT \simeq 25$ keV. Afterwards, d remains of the order of $\lambda\gamma$; that is, it increases very rapidly, because annihilation provides enough energy for the corresponding coalescence of baryonic condensations into larger homogeneous units.

To follow the evolution of the density and of d as a function of time, it is necessary to evaluate the rate of annihilation ν per unit of area of the boundary and per unit of time. In its full generality the problem is complicated, but simple results could be obtained in the following way. At the boundary between matter and antimatter, there is a region of overlap. In that region, the annihilation effect determines the mean free path of nucleons, so that their rate of annihilation is controlled by their thermal velocity. Because radiation pressure is dominant, no inhomogeneity in the local density of matter can develop[2] so that matter and antimatter flow towards their common boundary at the thermal velocity of the protons v. As a result

$$v = N\nu \qquad (9)$$

This gives only a small relative amount of annihilation during the coalescence period. Nevertheless, this annihilation is sufficient to provide enough energy to keep the equality $d = \lambda\gamma$ till the recombination period.

If one estimates the ratio η between the density of baryonic number and that of photons to be around 10^{-1} near the end of the separation period, one gets $10^{-12} < \eta < 10^{-8}$ at the time of recombination. Presumably the effect of coalescence stops then if only because the corresponding motion of the fluid would be supersonic.

The size of the emulsion and its density are found at that point to be $10^{21.5}$ cm and 10^{-20} g/cm^3 so that the average mass of a matter region is typically 10^{11} M; that is, of the order of a galactic mass.

I may also mention the new form taken by the problem of nucleosynthesis in such models[10]. Nucleosynthesis takes place during the leptonic era, in the emulsion of matter and antimatter which has at that time a very large density, similar to the densities which have been considered by Wagoner, Fowler and Hoyle[11] for the case of bouncing massive stars. The chief features of these high density expanding models are that they produce a large abundance of helium (equal amount in mass of H and He) and a relatively large amount of heavy elements but a small amount of low mass elements. During the intense annihilation after nucleosynthesis, most nuclei disappear. Protons and antiprotons are partly regenerated by H–$\overline{\mathrm{He}}$, $\overline{\mathrm{H}}$–He and $\overline{\mathrm{He}}$–He collisions. The present ignorance of the corresponding cross-sections does not yet enable us to calculate the resulting hydrogen/helium ratio.

Finally, such considerations suggest a revival of interest in the matter–antimatter model of quasars[12] and galactic nuclei. The arguments which were used to rule out this mechanism do not apply to the structures which evolve from the emulsion, that is, a compact mass of matter surrounded by antimatter or vice versa, in particular because they do not take into account the existence of magnetic effects.

To avoid misunderstanding, I stress that there are three aspects to the discussion of antimatter, namely the possibility of a phase transition in the black-body radiation, coalescence with galaxy formation and quasar models. None of them is necessarily associated with the other ones and the last two should be considered separately if one wants to discuss the experimental evidence for the existence or non-existence of antimatter.

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Effect of Oxidation on the Natural Remanent Magnetization of Titanomagnetite in Suboceanic Basalt

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The natural remanent magnetization of titanomagnetite is not destroyed by oxidation if the oxidation occurs below the original Curie temperature of the titanomagnetite.

THE palaeomagnetic memory of most igneous rocks resides in grains of magnetite and titanomagnetite which are chemically unstable. Under conditions of low temperature and high oxygen fugacity such as those which exist in rocks presently at the Earth's surface, titanomagnetite tends to oxidize to an equilibrium mineral assemblage of rutile and haematite, with intermediate formation of titanomaghemite, ilmenite, and iron-rich titanomagnetite[1]. The work reported here has been concerned with the magnetic changes resulting from the initial stages of such oxidation in submarine tholeiitic basalt. Of particular interest is the effect of submarine weathering on the magnetic remanence of submarine basalt, as well as the process by which basalt loses its remanence as it descends into the mantle.

Increases in the Curie temperature of basaltic rocks from high temperature oxidation have been observed both in the laboratory[2–5] and in nature[6]. An increase in Curie temperatures from the weathering of submarine basalts on the sea floor has also been reported[4,7]. The question of what happens to the natural remanence of basalt during oxidation, however, has received little attention. If the direction of the ambient magnetic field during oxidation is not parallel to the direction of the original natural remanence, it is important to know whether the rock will retain a magnetic memory of the original magnetization or whether it will become completely remagnetized in the direction of the ambient field.

The question of the temperature at which oxidation occurs is crucial. The Curie temperature of the oxidized mineral is usually greater than that of the original mineral and so oxidation takes place generally in one of the following three ways: (1) The oxidation occurs at a temperature greater than the Curie temperature of the oxidized mineral. When it cools, the rock acquires thermoremanent magnetization (TRM). (2) The oxidation temperature is between the Curie temperatures of the original mineral and oxidized mineral. Chemical remanence (CRM) is then the only type of remanence formed; it is parallel to the field acting at the time of the oxidation, which may occur either during initial cooling or during subsequent reheating. (3) The oxidation temperature is below the Curie temperature of the original mineral. Remanence of two types may result: (*a*) the original TRM may persist through the changes in lattice structure accompanying oxidation, or (*b*) new CRM may be produced in the ferromagnetic minerals formed by the oxidation, and this new CRM is controlled by the ambient field at the time of oxidation.

Our work was undertaken to determine whether any memory of the original NRM persists through the introduction of cation vacancies and changes in the crystal lattice during oxidation. We were also interested in the intensity of the CRM produced by oxidation, and its spectrum of blocking temperatures.

The samples used included six specimens from a suboceanic basalt sill drilled in the eastern Pacific near Guadalupe Island[2], two specimens from a basalt pillow dredged 20 km from the axis of the Juan de Fuca Ridge[8], and three specimens of pillows from the central rift valley of the Mid-Indian Ocean Ridge[8]. The opaque mineral in the pillow basalt was identified as titanium-rich titanomagnetite on the basis of its brownish colour, optical anisotropy, and low Curie temperatures, most of which were from 175° to 200° C. A Curie temperature of 325° C was measured in specimen 12–2, taken 2 cm below the surface of the Juan de Fuca pillow. Such a high Curie temperature is typical of the crusts of pillow basalts[9,10]. This same pillow fragment also has a weathered rim and the opaque grains in specimen 12–2 have a somewhat silvery reflectance that suggests partial oxidation. Specimens of the submarine sill also had high Curie temperatures and contained an oxidized magnetic mineral identified as titanomaghemite on the basis of its silvery reflectance and lattice spacing (cubic cell edge of 8.383 Å).

Experimental Procedure

The objective of the experiment was to observe changes in the NRM of the samples when they were heated in air and simultaneously to observe the growth of new CRM. We used an astatic magnetometer, which consisted of a pair of north–south astatic magnets suspended 7 cm above the sample, a rotating sample stage with a nonmagnetic furnace, and three pairs of Helmholz coils used both to cancel the Earth's field and to produce a known east–west magnetic field *H* (Fig. 1). The sample stage could be rotated about a vertical axis, so that any component of magnetization in the horizontal plane could be determined with a standard light beam system.

The key element in the design of these experiments was the alignment of the samples so that the NRM was exactly perpendicular to the applied field, *H*, during the heating. Because the resulting CRM and NRM vectors were orthogonal, their changes in intensity could be determined independently. Three steps were taken to ensure orthogonality during the experiment. First, samples were partially demagnetized at 100° C to ensure that they possessed only unidirectional NRM. The second step was to align carefully the astatic magnets so that they were exactly perpendicular to *H*. The third step was to use the condition of zero defection of the magnetometer to determine the exact orientation of the stage needed to place the NRM of the sample parallel to the astatic magnets and thus perpendicular to the applied field, *H*, during heating. After the experiments were completed, the remanent magnetization acquired on cooling in the east–west applied field was measured with a spinner magnetometer as a check on the initial alignment of the NRM in the astatic magnetometer. In all cases, the final TRM was perpendicular to the initial NRM within several degrees.

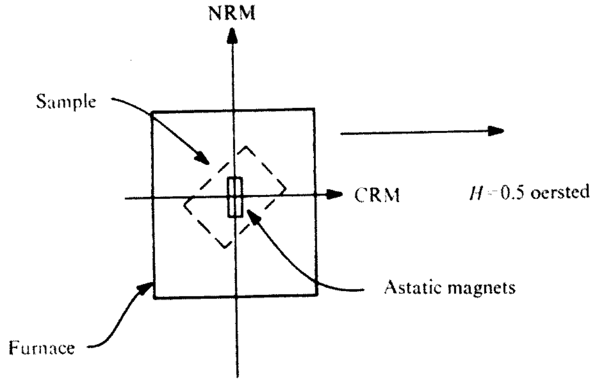

Fig. 1 Plan view of the experiment. During heating, the NRM of the sample was perpendicular to the applied field, *H*, and parallel to the astatic magnets. The field at the centre of the sample from the astatic magnets had an intensity of 0.01 oersted and a direction opposite to that of the NRM. New CRM due to oxidation of the titanomagnetite is assumed to form in a direction parallel or antiparallel to that of *H*.

A magnetic field *H* was maintained perpendicular to the NRM at all times during the course of the experiments except for brief intervals of 1–2 min, when it was switched off to permit measurement of the NRM and CRM. The intensity of *H* was adjusted to approximate to the field that existed at the sample sites when the lavas originally solidified, the assumption being that the field was that of an axial dipole with a moment of 8×10^{25} G cm^3.

After partial demagnetization at 100° C, the sample was held at a constant temperature of 250° C for a period of half an hour, during which the NRM and CRM were measured at 10 min intervals. The temperature was then rapidly raised about 50° C and a new set of measurements taken at 10 min intervals was made at constant temperature. Increases in the two orthogonal components of remanent magnetization which occurred during the intervals of constant temperature are due to chemical changes occurring at that temperature.

Experimental Results

A typical run on pillow basalt is shown in Fig. 2. On heating to 250° C almost all of the NRM was destroyed and no CRM was produced, indicating that destruction of NRM was by simple heating to the Curie temperature rather than by chemical change. Repeat measurements slightly below the blocking temperature disclosed no evidence of viscous demagnetization. Noticeable chemical change began with further heating, and reached a maximum of about 400° C. A large fraction of the CRM grown at any temperature was destroyed when the sample was heated through the next 50° C, indicating that the Curie temperatures and blocking temperatures of the new CRM were only slightly greater than the temperature at which the CRM had been created. Above 500° C the rate of production of CRM was small, presumably because by then the oxidation reaction had gone to completion. The maximum Curie temperature of the CRM was about 580° C, essentially that of magnetite. The final step in the experiment was to cool the oxidized rock in the same field, *H*, to produce the TRM curve shown in Fig. 2. The blocking temperatures of the oxidized rock were in general greatly increased and the intensity of the TRM was several times that of the NRM, which presum-

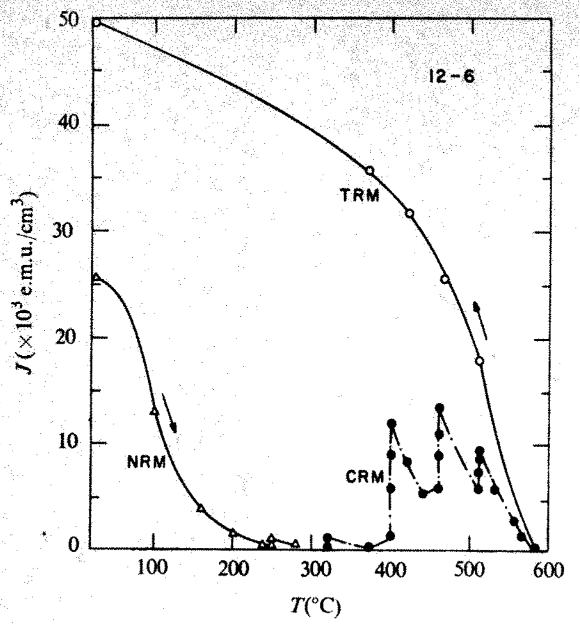

Fig. 2 Heating experiment in air on a sample in which oxidation occurs at a temperature above the Curie temperature of the original titanomagnetite. △, Changes in NRM; ●, CRM during oxidation; ○, acquisition of TRM by the oxidized rock. The temperature was held constant for 30 min at 250°, 320°, 400°, 460°, and 510° C with readings every 10 min. H was 0.50 oersted. Specimen 12–6 was taken 6 cm below the glassy surface of basalt pillow 12 from the Juan de Fuca Ridge[6].

ably was chiefly thermoremanence acquired in a field comparable with H. This experiment exemplifies the case (2) in which the Curie temperature of the original ferromagnetic mineral is very low and the oxidation occurs above that temperature.

In other samples with higher initial Curie temperatures, oxidation corresponding to case (3) began before the Curie temperature of the NRM was reached (Fig. 3). The heating experiments on these samples establishes clearly that the NRM was not destroyed by the oxidation but rather that it increased in intensity during isothermal oxidation. The increase was probably due to an increase in spontaneous magnetization of domains with walls pinned by energy barriers that were not destroyed by the oxidation. The increase in NRM occurred over a slightly lower temperature range than the growth of CRM, the maximum increase in NRM occurring at 300° C. As was true of the CRM, part of the NRM which survived oxidation was destroyed on being heated several tens of degrees above the temperature at which the oxidation had occurred.

Oxidation first became measurable in these samples at temperatures between 200° and 300° C. Oxidation was favoured by open rock textures through which diffusion of air was more rapid and possibly by the presence of hydrated clay minerals which, when heated, produced water vapour that dissociated to produce oxygen. The effect of increasing the temperature was to increase the rate of oxidation. Where this occurred at temperatures above the Curie temperature of the original titanomagnetite (case (2)), CRM was produced parallel to the applied field. This magnetization was formed as the blocking temperature of the oxidizing titanomagnetite rose above the ambient temperature.

Where measurable oxidation began below the Curie temperature of the original titanomagnetite (case (3)), the NRM was changed by the rather complex sequence of events seen in Fig. 3. Two competing processes are evident: heating, which tended to destroy the NRM as the temperature rose through the initial range of blocking temperatures; and oxidation, which tended to increase the NRM by increasing the spontaneous magnetization and to preserve the NRM by raising the blocking temperatures. The NRM was not destroyed evidently because the energy barriers that pin domain walls persisted through the oxidation. CRM was formed in domains heated above their blocking temperatures during a temperature increment as the result of partial oxidation which raised the blocking temperature above the ambient temperature.

What do these experiments tell us about the magnetic changes to be expected in rocks as they undergo incipient oxidation by natural processes? Theoretically CRM can be formed by either of two processes. If the ambient temperature during oxidation is higher than the initial blocking temperature of the magnetic material, a large amount of CRM is produced as the blocking temperatures rise above the ambient temperature (specimen 12–6). This process is probably not common in nature, however, where oxidation due to weathering takes place at a temperature far below the blocking temperature of titanomagnetite. Moreover, oxidation due to low grade metamorphism that occurs as rocks are slowly heated during burial is a gradual process which probably begins before the Curie temperature of titanomagnetite is reached. Initial oxidation during weathering or burial thus occurs generally below the Curie temperature, where CRM is formed as new energy barriers are created which pin domain walls. The intensity of the CRM created in this way, however, can be no larger than about a fortieth of the value of the induced magnetization. We conclude therefore that most of the natural remanence in partially oxidized basalt is original remanence that has retained its direction through the oxidation. It is not new CRM formed during the chemical alteration.

The role of heating in these experiments was to increase reaction rates to measurable levels. There are undoubtedly differences between the magnetic effect of oxidation in the laboratory at a temperature of 300° C for several hours and oxidation on the sea floor at a temperature of 0° C for millions of years. As evidence of this difference, the intensity of magnetization of submarine basalt has been observed to decrease with increased weathering[7], rather than to increase as in our experiments. Yet our conclusion that titomagnetite retains a memory of its original magnetization after oxidation offers an explanation for the existence of coherent marine magnetic anomalies produced by parts of the sea floor that are at least 70 m.y. old and which are now partially oxidized. The present results do not offer a ready explanation for the sudden disappearance of the magnetic anomalies at the oceanic trenches,

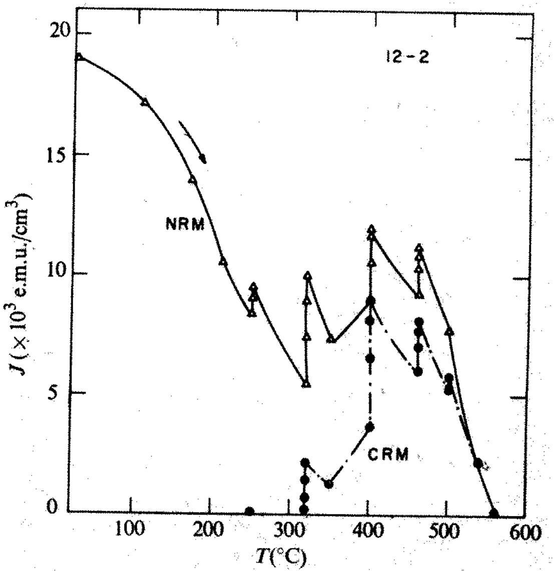

Fig. 3 Heating experiment in air on a sample in which oxidation began at a temperature below the Curie temperature of the original magnetic mineral. Other symbols as in Fig. 2. Specimen 12–2 is from the same pillow as the specimen shown in Fig. 2, but was taken 2 cm below the glassy surface of the pillow.

which probably reflects the complete destruction of the cubic magnetic minerals due to an acceleration of metamorphic reaction rates during burial and tectonic deformation.

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Polywater and Polypollutants

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Some careful experiments and a close look at the literature of polywater give no reason to believe that any new phenomenon has been discovered. Contamination could account for the observed effects.

THE concept of an entirely new species of water (known variously as polywater, water II, or anomalous water) owes its publicity principally to Derjaguin[1] and his co-workers. Their conclusions have been based on their own experimental work on the physical properties of water condensates in fine glass capillaries, and also on the earlier indicative observations by independent workers (for example, ref. 2). Derjaguin[1] in his latest article has reviewed his experimental work and confirmed that he still strongly believes in this new water species which, he claims, has abnormally high values for the molecular weight, viscosity (ten to twenty times greater), refractive index (1.48), boiling point (above 150° C) and anomalous density–temperature characteristics below room temperature. It has long been known that surface forces can greatly modify the properties of adjoining water layers. Derjaguin himself could be said to be the principal pioneer of this work during the past 20 years or so, for which he has justifiably obtained universal recognition. It must be stressed, however, that his water II phenomenon is of a completely different order from this, for he claims that water II can exist independently of the surface from which it has been catalytically formed. He claims that it does not lose its anomalous properties unless vaporized above 700° C. In the early days of these investigations he discussed the problem with J. D. Bernal (early 1968) and of his difficulty in getting the work recognized. Bernal's continued ill-health prohibited him from doing any really active research himself on the topic, and he left it to us to carry out the investigations under his general guidance.

If Derjaguin's chief contentions are correct, the problems facing the physical chemist are prodigious. He must interpret water II in terms of a completely new type of hydrogen bond which nevertheless can be easily formed during the condensation of slightly undersaturated vapours on to the appropriate surface. He must also explain why ordinary water—less stable than water II—is the predominant form in nature. Not surprisingly, Derjaguin found it difficult to convince other scientists, and a man of lesser reputation would have surely failed to do so. However, his continued assertions led many groups in the western world (notably in Britain and the United States) to follow up his work. These groups produced results which seemed to both confirm and contradict his findings. Furthermore, several theoreticians (for example, refs. 3-9) actively pursued the problem of determining a suitable quantum mechanical picture for the new bonding required to explain the anomalous properties; needless to say, some of these models were highly speculative[10].

The evidence against the concept of water II has mostly accumulated very recently. Briefly, the contention is that the effects of even small amounts of certain impurities incorporated in the minute (say 10^{-10} to 10^{-5} g) samples have been underestimated. Derjaguin's defence of water II may seem impressive, but we believe that his account gives, however unintentionally, an incomplete presentation of the facts, and in view of its possible wide influence we feel we must state clearly our findings. We therefore wish to explain how our work and of others have led us to reject water II as a real phenomenon, and to examine more critically some of the claims of Derjaguin and his supporters.

The Phenomenon

Our investigations have been in progress for the past 2.5 years and we have used all known methods of production as well as introducing many modes of our own. Fuller details of this work are being prepared for publication later. (We have too much material to be included here, but some of our results have been mentioned by Hasted[11].) The degrees of anomality in our samples were determined chiefly from observations on (i) the phase separation effects[1], (ii) the gel-like residue obtained after evaporation, and (iii) the shape of the density–temperature curve obtained after certain corrections had been made for the effect of the narrow capillary bore. The method of production was continually refined so as to eliminate as many sources of contamination as possible. For example, before using a water pump (rather than a rotary pump) method, the residues obtained showed a higher carbon content as revealed by electron microprobe analysis and advanced mass spectrometric techniques. It was generally established that the degree of anomality usually diminished as the apparatus and techniques were refined. We have now produced samples which are indistinguishable from ordinary pure water.

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As a result of our studies and with some knowledge of the experiments of other workers, we have concluded that the most common sources of contamination in the general production of anomalous water are as follows (not in order). (1) Gross salt contamination, by surface migration and/or vapour transport, when salt solution (for example, K_2SO_4 or NaCl) methods of production are used. (2) Capillary residues (for example, nitrogenous or silicaceous) resulting from the capillary "cleaning" process. (3) Leaching out of the intrinsic glass components (silicon, sodium and so on) from the capillary walls. (4) Surface migration and vapour transport of contaminants inherent in the apparatus; for example, (i) greases from joints, "O"-rings, insufficiently cleaned glassware, and sample handling; (ii) residues arising from chemical cleaning of the apparatus (as in 2); (iii) back-streaming of rotary pump oil vapours even with the use of cold traps; (iv) resident apparatus gases such as carbon dioxide; (v) gaseous or organic impurities located at apparatus occlusions, dust particles and so on.

Several groups have used the salt solution method, and their results must therefore be immediately discounted. Of those remaining, we wonder which apparatus could genuinely be claimed to be free of even the grease sources mentioned in (4i). The leaching products (source 3) are, of course, mostly unavoidable, and this, we believe, is why so much attention has been directed to identifying silicon as the principle impurity in anomalous water[12–15]. These contentions, however, of which most are based on little more than circumstantial evidence, are in complete contradiction with the facts. In the literature[16–20] and in our own work, impurity tests (most of which involve electron microprobe techniques) clearly show, with one exception[14], that silicon is either absent or present in amounts that are minute compared with other "offending elements". Yet publications persist in alluding to silicon. We stress this point because we believe it partly explains the long time taken to recognize water II as an impurity effect—people have been suspecting the wrong impurities. In the final analysis, the real offending impurities are those of source (4)—particularly the organic impurities emanating from apparatus occlusions and even the sample handling in some cases[20]. (It is worth noting that silicon vapours arising from the vacuum pump oil could also be present.) This is in keeping with the known facts on impurity tests (refs. 16–20 and our own work) in which organic substances (lipids and phospholipids) and the elements carbon, sodium, potassium, chlorine, sulphur (in rough order) notably appear in varying degrees of prominence. Even among the work supporting water II, Derjaguin's samples are recognized to contain organic impurities (see later) and Lippincott *et al.*[4] admit to a small percentage of sodium and an unknown amount of carbon (see also other comments[19,22] on the work of Lippincott *et al.*).

For and Against Polywater

It has been well established from the work of others and ourselves that the macroscopic and microscopic properties of water in fine capillaries can be greatly modified by the controlled addition of certain impurities. Indeed it has been demonstrated that (i) anomalous phase separation and density–temperature profiles can be obtained (refs. 12, 16, 18 and our own work) with solutions containing various salts, pump oils, silicon, hydrosols and other additives, such as Na and B, which leave their characteristic residues after evaporation of the ordinary water; (ii) the published infrared spectra of polywater have a strong resemblance to those of a number of chemical solutions[16–18,20–23] including carboxyl groups, bicarbonates, sulphates, sodium tetraborate, sodium and potassium nitrate, and particularly nitric acid and also human sweat. There can be little doubt that all the reported properties of anomalous water can be reproduced using an appropriate choice of additives. Clearly the exact impurity composition between different experiments and even between different samples must vary as do the reported properties of anomalous water. It is worth noting that different workers also use different concentrations; some use a very dilute mixture that exists before complete evaporation while others use only the residue.

On the question of organic impurities, Derjaguin seems content to deduce from the analysis in collaboration with V. L. Talrose that "one *can state* that the amount of organic compounds one *can consider probable* in the columns of water is much smaller than the amount *necessary to explain* the marked differences from normal water" (our italics). Apart from the vague wording of this statement, two important issues are involved. First, implicit in Derjaguin's thinking is that, if a certain concentration of impure water in bulk does not deviate from ordinary water, this will be true for the same concentration of impure water in fine capillaries (note that he uses this type of assumption with his "quartz powder experiment"). Knowing the considerable work (much of it by Derjaguin himself) on the restructuring capabilities of both surfaces and impurities (see refs. 24 and 25), ought one to expect the microscopic properties of impure solutions in fine capillaries to be reflected in the bulk state? Here Derjaguin seems to be in danger of falling into a pit of his own making. Second, the implication in the statement that the impurity concentration is small has certainly not been supported by analysis. According to Davis[20], the analysis of Talrose on Derjaguin's samples revealed enormous concentrations of organic substances (not unlike human sweat). Derjaguin, however, does not mention this.

Derjaguin's experiments cover many years of work using several methods of production. He talks of purity tests in connexion with a later purer apparatus, yet as far as we know all his published data stem from work with the earlier impure apparatus. This point is vital and must be clarified.

On more specific points too there seem to be several implicit contradictions. The dexterity used in the surface tension measurements was apparently sufficient to detect a 3% rise for water II concentrations of 20% by weight! Yet elsewhere he dismisses another experiment (the effect of pertubation on viscosity) simply as having "assigned too much weight to the result". In addition, we wonder how the viscosity results might be affected by the "spontaneous motion" effect—an effect that Derjaguin later describes as the sudden motion of an anomalous column when closer to one end of a capillary (that is, as it would be in a viscosity measurement). Also, how are these effects (and others like "daughter column production", distillation and so on) affected by the surface migration and vapour transport of both water and impurities? We know from the experiments of others[16,17] as well as ourselves that these factors cannot be neglected. One could raise many more objections specifically aimed at individual experiments. However, for brevity here, we must regard them as of minor importance compared with issues already mentioned.

Derjaguin cites work in progress in the United States, Britain and Belgium to support his case. In fact his supporters are in a minority. Lippincott *et al.*, as we have shown, admit to the presence of impurities in addition to carbon, and their infrared spectra suspiciously resemble those of several solutions, particularly nitric acid. The work of Pethica *et al.*[26] which Derjaguin regards as partially confirmatory is no longer regarded as such by at least one of the authors[15]. Our early (impure) work too could have been said to have confirmed Derjaguin's results.

Is it conceivable that Derjaguin and his collaborators alone have found the formula for producing pure anomalous water, while all others at best make impure imitations? Were this so, then, by virtue of the apparent ease of its production in 100 µm capillaries (production time of only 1 h or so), the ease of its distillation from small capillaries into a larger tube, and its great stability, this would make anomalous water an ideal substance for collective preparation. If this were so, a simple calculation shows that in the years of Derjaguin's experiments the production of a beaker full or even test-tube full of the substance should present no problem. Such a sample could then be made available for rigorous widespread examination.

Some of the work supporting the case for anomalous water may at first seem impressive. Closer examination, however, shows that much of the published work is careless, inconclusive and often misleading, if not wildly conjectural. Our final conclusions are: first, the observed properties of so-called anomalous water are simply the result of either gross impurities or impurity effects enhanced by surface proximity. Second, if sufficient precautions are taken to eliminate the appropriate contaminants, then the capillary products can become indistinguishable from ordinary water. Third, the different anomalous properties reported merely reflect the different types and levels of impurities characteristic of the methods of preparation. Fourth, although one can never dogmatically deny the existence of something not obtained, we think it highly unlikely that a pure anomalous water can exist.

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Purification of an Altered DNA Polymerase from an *E. coli* Strain with a *pol* Mutation

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DNA polymerase purified from an *E. coli* strain with a *pol* mutation has been shown to differ from purified wild type enzyme in several characteristics. This result demonstrates that the *pol* gene is the structural gene for DNA polymerase.

CELL-FREE extracts from the *Escherichia coli* mutant *polA1*, which has been isolated by De Lucia and Cairns[1], incorporate less than 1% as much deoxynucleoside triphosphate into acid-precipitable material as extracts of the parent strain in identical conditions. Although the mutation has been mapped and is an amber mutant[2], there is as yet no direct proof that the *polA1* lesion is actually in the structural gene which codes for DNA polymerase. The mutation might therefore increase the level of some nuclease, thereby destroying the product of the polymerase (although this is unlikely because *polA1* is recessive[1,2]); it might affect the extraction of the enzyme, although not its structure *in vivo*; or a promoter element might be mutated so as to produce fewer polymerase molecules of unaltered structure.

Moses and Richardson (personal communication) have been unable to detect any abnormality of the DNA polymerase purified from several suppressed derivatives of the amber *polA1* mutation. Cairns and De Lucia (personal communication) have isolated five additional *pol* mutants, and transduction with phage P1 has shown that these map at the same site on the chromosome as *polA1*[3]. Preliminary studies in this laboratory (Peacey, personal communication) have shown that extracts of one of these mutants, *pol-6*, prepared by sonic disruption, contain about 20% of wild type DNA polymerase activity, which is partially destroyed by preincubation at temperatures which have little effect on wild type extracts. The *pol-6* cells do not themselves seem to be temperature-sensitive in their growth or in the methylmethane sulphonate (MMS) sensitivity characteristic of all *pol* mutants[3].

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We have found that, unlike the wild type enzyme, the DNA polymerase partially purified from *pol-6* cells is less active when assayed at 52° C than at 37° C. We have therefore purified the enzyme from *pol-6* cells, and report now that the purified enzyme retains this property, as well as differing in other ways from wild type enzyme. This demonstrates that the *pol* mutation is in the structural gene for DNA polymerase.

Large Scale Purification

We have purified DNA polymerase according to published procedures[4,5] using batches of log phase cells. The enzyme from wild type *E. coli* K-12 was first purified from 600 g of cells. The purified enzyme fraction (fraction VII) amounted to 4.4 mg of protein, which was essentially homogeneous when analysed in SDS-polyacrylamide gel electrophoresis (Fig. 1). This polymerase preparation was highly active in the assay system described by Richardson, Schildkraut, Aposhian and Kornberg[5]; its properties were exactly the same as those described by the previous investigators[4,5] for the enzyme purified from *E. coli* B.

We have used the same protocol to purify polymerase from several batches of *pol-6* cells. In each case, the MMS sensitivity of the cells was tested at the time of collection. The polymerases from wild type and *pol-6* cells fractionated in an identical manner during the first five steps of the purification (Table 1), which resulted in a twenty to forty-fold increase in specific activity in each case. The absolute specific activities of the *pol-6* fractions were consistently lower than the corresponding wild type fractions (Table 1).

The behaviour of the two enzyme preparations differed significantly in step VI of the purification[4], which consists of elution with a potassium phosphate gradient from a phosphocellulose column (Table 1). Fig. 2 shows phosphocellulose chromatograms of fraction V of wild type and mutant extracts. The wild type polymerase activity, indicated by histogram bars, elutes in the gradient fractions which contain a major protein peak. In contrast, the *pol-6* polymerase appears in fractions with a slightly greater phosphate concentration. The R_Fs of elution with respect to the phosphate gradient were 0.34 for wild type and 0.36 for *pol-6* polymerase. This difference is small but reproducible. Although we did not find any significant losses of wild type polymerase, as much as two-thirds of the mutant polymerase activity was lost in the column front. This material had the same low specific activity and sensitivity to high temperatures as the materal applied to the column and as the fractions of peak activity eluted from it. When it was rechromatographed it behaved identically. We do not at present understand the basis for this phenomenon.

Fraction VI was further purified by chromatography through a column of 'Sephadex G-150' (Table 1, fraction VII). Although the procedure of Jovin *et al.*[4] utilizes a column of 'Sephadex G-100' for preparation of fraction VII from wild type cells, we chose the larger pore size to try to achieve a better separation of *pol-6* polymerase from the impurities found in the phosphocellulose fractions at $R_F = 0.36$.

In the final purification steps the wild type and mutant preparations differ markedly in their response to poly dAT and calf thymus DNA as templates. Poly dAT is a much

Table 1 Purification of DNA Polymerase from Wild Type *E. coli* K-12 and from the *pol-6* Mutant

Fraction	Protein (mg/ml.)	Specific activity at 37° C*	Assay template	Ratio of activities at 51° C and 37° C
		A, Wild type		
I Crude	20	3.7	Calf thymus DNA	1.6
II Streptomycin	16.8	14.7	Calf thymus DNA	1.5
III Autolysis	2.9	—	Calf thymus DNA	—
IV Ammonium sulphate	19.4	203	Calf thymus DNA	1.4
V DEAE cellulose	8.6	166	Calf thymus DNA	1.8
		360	poly dAT	1.6
VI Phosphocellulose	3.6	4,200	poly dAT	1.3
VII 'Sephadex G-100'	2.7	330	Calf thymus DNA	1.7
		3,000	poly dAT	2.4
		B, *pol-6*		
I Crude	19.0	1.7	Calf thymus DNA	0.4
II Streptomycin	5.6	3.5	Calf thymus DNA	0.4
III Autolysis	3.0	6.7	Calf thymus DNA	0.4
IV Ammonium sulphate	14.0	33.3	Calf thymus DNA	0.4
V DEAE cellulose	5.0	52.8	Calf thymus DNA	0.33
		3.1	poly dAT	—
VI Phosphocellulose	4.35	30	Calf thymus DNA	0.24
		2.8	poly dAT	—
VII 'Sephadex G-150'	1.76	70	Calf thymus DNA	0.60
		14	poly dAT	0.33

The assays were modified from the proportions described by Richardson *et al.*[5]. Assays were conducted at 37° C or at 51° C for 30 min.

Assay with calf thymus DNA template: 6.54 nmol dGTP, dCTP and dTTP; 3.26 nmol ^{3}H-dATP (2×10^{-2} Ci/mol); 1.63 µmol $MgCl_2$; 0.33 µmol mercaptoethanol; 5.76 µmol glycine *p*H 9.2 and 0.26 nmol "activated" calf thymus DNA † plus enzyme ‡; total volume of 0.20 ml. Assay with poly dAT template: 9.5 nmol dTTP, 4.75 nmol ^{3}H-dATP (1×10^{-2} Ci/mol), 2.36 µmol $MgCl_2$, 0.475 µmol mercaptoethanol, 20 µmol potassium phosphate *p*H 7.4, 3.57 nmol dAT copolymer plus enzyme; total volume of 0.20 ml. Each assay was tested for linearity of ^{3}H-dATP incorporation with time by removing 50 µl. samples at zero time and every 10 min thereafter. These samples were spotted on Whatman 3MM filter paper disks which were washed thoroughly with cold 5% trichloroacetic acid (TCA) containing 1% sodium pyrophosphate. The TCA was extracted with ethanol and the disks were dried. Radioactivity retained on the disks was estimated by counting them in a liquid scintillation counter. This method is a modification of that of Bollum[7]. Deoxyribonucleoside triphosphates and calf thymus DNA were obtained from Calbiochem; poly dAT from Miles; ^{3}H-dATP from Schwarz Bioresearch; other materials from standard laboratory supply houses.

* Specific activities are expressed as an arbitrary unit proportional to the net number of ^{3}H atoms incorporated into TCA precipitable material in 30 min at 37° C per mg of enzyme protein.

† Activated calf thymus DNA was prepared by limited nuclease digestion of the DNA with pancreatic DNAase as described by Richardson[8].

‡ The enzyme was diluted with the Tris-ammonium sulphate–mercaptoethanol–bovine serum albumin buffer described by Richardson *et al.*[5].

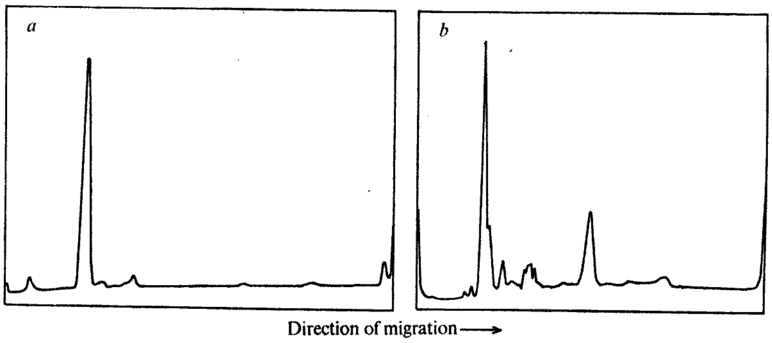

Fig. 1 Densitometer tracings of SDS-polyacrylamide gels after electrophoresis of purified DNA polymerase preparations. SDS-polyacrylamide gels were prepared, run and stained according to the procedure of Weber and Osborn[6]. After destaining, the gels were scanned directly using a Joyce–Loebl ultraviolet scanning densitometer. Migration of the protein is from left to right of the figure. *a*, 14 µg of wild type DNA polymerase fraction VII. Full scale A_{260} is 2.0. *b*, 18 µg of *pol-6* DNA polymerase fraction VII. Full A_{260} is 1.0.

better template than calf thymus DNA for the wild type enzyme in fractions VI and VII[5], whereas it is a very poor template for the mutant enzyme fractions (Table 1). This means that calf thymus DNA must be used to assay these fractions from *pol-6* cells, so that little purification seems to be achieved in the final steps. But the same is true of the wild type preparation if calf thymus DNA is employed in place of poly dAT.

The mutant enzyme remains sensitive to high temperature throughout its purification. The ratio of activity at 51° C to that at 37° C varied between 0.24 and 0.60 for the *pol-6* enzyme; and between 1.3 and 2.4 for the wild type fractions, as shown in Table 1.

Behaviour of the *pol-6* Polymerase

A comparison of the properties of enzyme fractions from *pol-6* and wild type cells shows that the *pol-6* enzyme represents a slightly modified form of DNA polymerase. The possibility that the low specific activity of the mutant preparation results from a highly effective nuclease rather than an inefficient polymerase can be tested by mixing experiments. First, crude extracts of the two types of cells were mixed and assayed together. Second, fraction VII of wild type polymerase was assayed in the presence of each of the seven fractions of the *pol-6* enzyme. In no case did the mutant enzyme fractions inhibit wild type activity. In addition, the higher specific activity of the wild type enzyme at 51° C was maintained in the presence of the mutant enzyme. Table 2 summarizes the results of such a mixing experiment for the two final fractions.

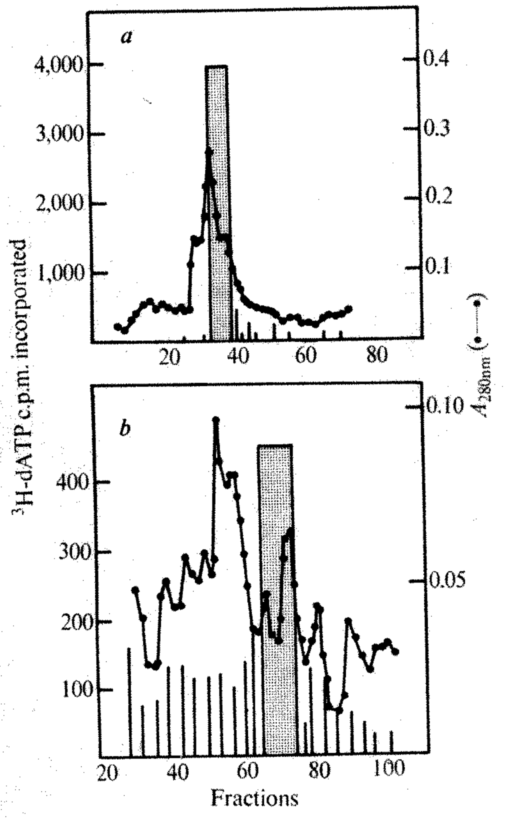

Fig. 2 Phosphocellulose chromatograms of fraction V of wild type (*a*) and *pol-6* (*b*) DNA polymerase preparations. Phosphocellulose chromatography of the DNA polymerase fraction V was carried out as described by Jovin *et al.*[4]. The protein was eluted from the phosphocellulose columns with a gradient of potassium phosphate *p*H 6.5. Fractions were collected and their absorbance at 280 nm was measured. Dilutions of these fractions were then tested for DNA polymerase activity using the assay system described in Table 1. The fractions containing DNA polymerase activity were pooled for further purification as fraction VI; their aggregate activities are indicated as a single histogram bar in each case. The histogram bars represent counts per minute of ^{3}H-dATP incorporated at 30 min in the assay of that particular fraction. . — . — represents A_{280}.

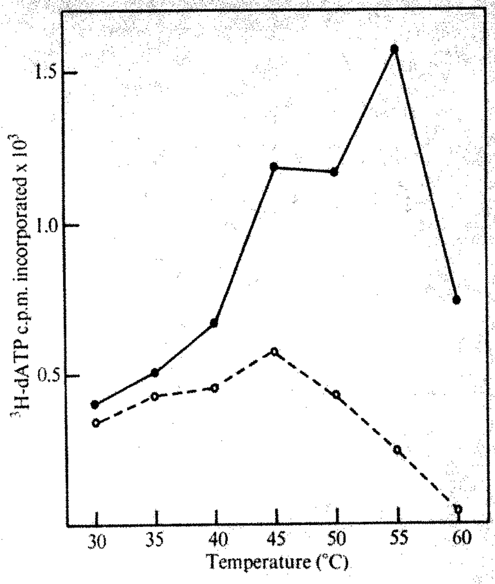

Fig. 3 Temperature profile of enzyme activity of wild type and *pol-6* DNA polymerase fraction VII. The purified DNA polymerase from wild type and *pol-6* was assayed with the calf thymus DNA primed assay described in Table 1 at temperatures between 30° C and 60° C. The final concentration of wild type polymerase in the assay was 0.1 µg/ml., that of the *pol-6* polymerase was 0.7 µg/ml. The incorporation of ^{3}H-dATP into TCA precipitable material after 30 min is plotted against the temperature. ●—●, Wild type incorporation; ○ - - - ○, *pol-6* incorporation.

The temperature optima of the purified enzymes were determined by assaying with calf thymus DNA as template over the range 30° C to 60° C. Fig. 3 summarizes our data. The wild type polymerase shows maximal activity at 55° C, whereas the optimum for the *pol-6* polymerase is 10° C lower.

The *pol*-6 polymerase is immunologically similar to wild type DNA polymerase. Both enzymes react with antiserum against wild type *E. coli* B polymerase in complement fixation tests, and their enzyme activity is blocked by incubation of the reaction mixtures in the presence of antiserum. We measured the conformation and stability of the enzymes by a sensitive complement fixation procedure[9], which showed that the melting temperature of the *pol-6* enzyme is 5° C lower than that of the wild type enzyme. These data indicate that there are basic similarities in the structure of the wild type and mutant enzymes but that they differ in conformational detail.

Table 2 Mixing Experiment using Fraction VII Polymerase from Wild Type *E. coli* and the *pol-6* Mutant

Enzyme	Final enzyme concentration (µg/ml.)	Template	^{3}H-dATP incorporation (c.p.m.) at 37° C	^{3}H-dATP incorporation (c.p.m.) at 51° C	Ratio 51° C/ 37° C
(*a*) Wild type	0.102	Calf thymus DNA	373	1,026	2.8
		poly dAT	453	793	1.7
(*b*) *pol-6*	0.730	Calf thymus DNA	511	413	0.8
		poly dAT	75	9	0.12
(*c*) Mixture of wild type + *pol-6* polymerases	0.102	Calf thymus DNA	1,107	1,538	1.4
		poly dAT	444	806	1.8
(*d*) Sum of (*a*)+(*b*)	0.730	Calf thymus DNA	884	1,439	1.6
		poly dAT	548	802	1.4

The purified polymerases from the wild type and the *pol-6* mutant were assayed separately and as a mixture at both 37° C and 51° C. Final concentrations of the two enzymes in the mixture, (*c*), were the same as in the assays of the individual enzymes, (*a*) and (*b*). The incorporations in the individual assays were summed, (*d*), for comparison with the results of the assay of the mixture.

Kornberg and Gefter[10] have recently isolated a DNA polymerizing enzyme in soluble form from *polA1* cells. It is most unlikely that this is the enzyme we have purified from *pol-6* cells. Their enzyme depends on the presence of ATP for activity in crude extracts, and catalytic activity is only abolished by concentrations of anti-DNA polymerase serum in a hundred-fold excess of that needed to block the wild type enzyme. By contrast, the activity in *pol-6* extracts can be assayed in the absence of ATP, and the purified product reacts strongly with anti-DNA polymerase.

We believe that our results demonstrate that the *pol-6* mutation is in the structural gene for DNA polymerase. The exact nature of the structural change that has resulted from the mutation is not clear at present. Our present data imply that only slight conformational changes are involved, but confirmation of this requires further experiments. Gross and Peacey (personal communication) have recently isolated an F′ factor carrying the amber *polA1* mutation and have shown that the F′ factor does not complement the polymerase defect in *pol-6* cells. It is therefore probable that *polA1* is also a mutation of the structural gene for DNA polymerase.

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Novel Species of tRNA

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A species of $\mathrm{tRNA^{Gly}}$ from *Staphylococcus epidermidis*, which participates in peptidoglycan synthesis but not in protein synthesis, has been purified to homogeneity. It contains only a single modified base, 4-thiouridine.

In certain species of bacteria, aminoacyl-tRNA apparently serves multiple synthetic roles. In addition to its familiar function in protein synthesis, it provides the amino-acid residues forming the interpeptide bridge of some bacterial cell walls[1-4]. Still other unusual functions of aminoacyl-tRNAs are their roles in aminoacyl phosphatidylglycerol synthesis[5,6] and in the terminal addition of amino-acid residues to proteins[7,8].

In the peptidoglycan of the cell wall of *Staphylococcus aureus*, the interpeptide bridge is pentaglycine, while in *S. epidermidis* both glycine and serine residues are found. For both glycyl-tRNAs from *S. aureus*[9] and the seryl-tRNAs from *S. epidermidis*[2], multiple isoaccepting species can be separated and all species function in peptidoglycan synthesis; but in each case a species of tRNA fails to participate in protein synthesis. We now report a study of the isoaccepting species of $\mathrm{tRNA^{Gly}}$ from *S. epidermidis* and find a parallel situation. Again there is one species ($\mathrm{tRNA^{Gly}_{I}}$) which functions only in peptidoglycan synthesis.

Isoaccepting Species of $\mathrm{tRNA^{Gly}}$

Crude tRNA from *S. epidermidis* was resolved into three fractions by chromatography on DEAE-cellulose (Fig. 1). The first fraction ($\mathrm{tRNA^{Gly}_{I}}$) eluted ahead of the main absorbance peak and after rechromatography on hydroxylapatite (Fig. 2), gave a major peak of ultraviolet absorbing material coincident with glycine acceptance. This material had a specific activity of 1,300 pmol of glycine (accepted per absorbance unit.

The second fraction ($\mathrm{tRNA^{Gly}_{II}}$) was further resolved into two peaks ($\mathrm{tRNA^{Gly}_{IIA}}$ and $\mathrm{tRNA^{Gly}_{IIB}}$) by chromatography on DEAE-cellulose at *p*H 5.0 (Fig. 3), while the third fraction ($\mathrm{tRNA^{Gly}_{III}}$) has not been further resolved during extensive purification.

All four isoaccepting species participated in the incorporation of ^{14}C-glycine into the interpeptide bridges of the peptidoglycan (Table 1).

Two messengers have been used to test participation in protein synthesis *in vitro*. Phage f2 RNA has been used such that the phage coat protein is the predominant product, and also phage T4 RNA, which codes for various proteins. With both messengers, glycyl-$\mathrm{tRNA^{Gly}_{IIA}}$, glycyl-$\mathrm{tRNA^{Gly}_{IIB}}$ and glycyl-$\mathrm{tRNA^{Gly}_{III}}$ function in the incorporation of glycine into protein. But in the same conditions, we could not demonstrate the incorporation of glycine from glycyl-$\mathrm{tRNA^{Gly}_{I}}$ into protein using either messenger (Table 2). Glycyl-$\mathrm{tRNA^{Gly}_{I}}$ did not inhibit the *in vitro* assay because its addition to each of the other $\mathrm{tRNA^{Gly}}$ species failed to suppress incorporation from those species.

The trinucleotide-dependent binding of ^{14}C-glycyl-$\mathrm{tRNA^{Gly}_{I}}$ to *Escherichia coli* ribosomes was not stimulated by the addition of the known glycine codons GGU, GGC, GGA, GGG. In identical conditions the binding of the other species of $\mathrm{tRNA^{Gly}}$

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Table 1 Utilization of ^{14}C-Glycyl-tRNA$^{\rm Gly}$ Species for Peptidoglycan Synthesis

Conditions	^{14}C-Glycyl-tRNA$^{\rm Gly}$ (Total c.p.m. added)	Radioactivity incorporated into peptidoglycan (% incorporation)
Complete	tRNA$_{\rm I}^{\rm Gly}$ (9,500)	713 (7.5%)
Minus UDP-GlcNAc		66
Complete	tRNA$_{\rm IIA}^{\rm Gly}$ (9,000)	460 (5.1%)
Minus UDP-GlcNAc		70
Complete	tRNA$_{\rm IIB}^{\rm Gly}$ (8,000)	527 (6.6%)
Minus UDP-GlcNAc		85
Complete	tRNA$_{\rm III}^{\rm Gly}$ (10,000)	540 (5.4%)
Minus UDP-GlcNAc		100

Assay of peptidoglycan synthesis was carried out using the reaction mixtures described by Matsuhashi, Dietrich and Strominger[1].

to *E. coli* ribosomes was stimulated by one or more of these trinucleotides (Table 3).

Analysis of tRNA$_{\rm I}^{\rm Gly}$

Table 4 shows our analysis of the nucleosides obtained from tRNA$_{\rm I}^{\rm Gly}$ after enzymatic hydrolysis. It contained approximately equimolar amounts of uridine, guanosine, cytidine and adenosine. A single modified nucleoside, 4-thiouridine, was present in an amount equal to 0.65 residue per mol. No other minor nucleoside was detected in an amount greater than 0.1 residue per mol. Because dihydrouridine has no absorption at 260 nm, it could not be detected by this technique; its absence was established from the analysis of ^{32}P-labelled tRNA$_{\rm I}^{\rm Gly}$ (ref. 14). Although the total tRNA from a *Mycoplasma* species has been shown to be deficient in minor bases[15], this is the first isolation of a pure species of tRNA which is missing so many modified bases. Estimating terminal adenosine after alkaline hydrolysis[14] gave a value of 1,300 pmol per mol of tRNA, in agreement with the value obtained for glycine acceptance. This value suggests that the chain length is about 85 residues.

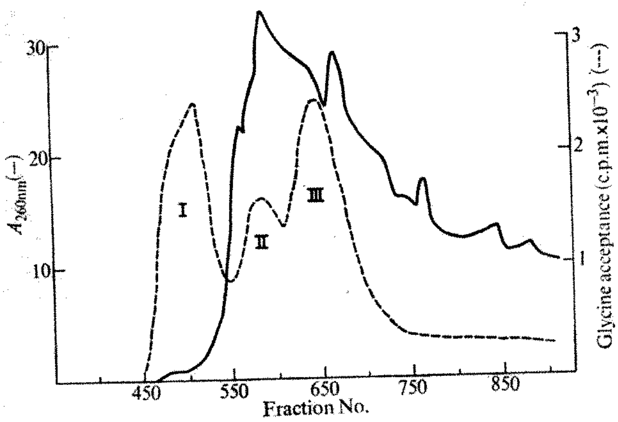

Fig. 1 Chromatography of crude tRNA from *Staphylococcus epidermidis* on DEAE-cellulose. Crude tRNA[2] (375,000 A_{260} units) in buffer (0.02 M Tris-HCl, *p*H 7.5, 0.001 M $MgCl_2$, 0.005 M $Na_2S_2O_3$, 0.001 M EDTA) was applied to a column of DEAE-cellulose (Whatman DE-52), 100×6 cm, equilibrated with the same buffer. Elution was carried out with 16 l. of a linear gradient from 0.25 M to 0.45 M NaCl in the same buffer. Fractions of 20 ml. were collected and assayed for glycine acceptance using 0.025 ml. of a column fraction, 7 μmol of HEPES (*p*H 8.0), 0.55 μmol of $MgCl_2$, 0.11 μmol of ATP, 0.2 μmol of 2-mercaptoethanol, 0.0085 μmol of mixed amino-acids minus glycine, 0.0016 μmol of ^{14}C-glycine (116 mCi/mmol, New England Nuclear Corp.) and 0.005 ml. of a crude enzyme preparation in a total volume of 0.08 ml. After incubation at 25° C for 30 min, trichloroacetic acid insoluble radioactivity was determined by standard procedures.

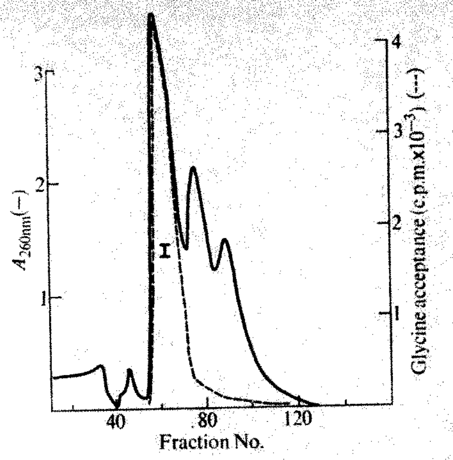

Fig. 2 Rechromatography of crude tRNA$^{\rm Gly}$ on hydroxylapatite. Crude tRNA$_{\rm I}^{\rm Gly}$ (2,200 A_{260} units), as eluted from the DEAE-cellulose column (Fig. 1), was applied to a column (100×2.5 cm) of hydroxylapatite[10], equilibrated with 0.05 M sodium phosphate, *p*H 6.88. Elution was carried out with 3 l. of a linear gradient from 0.08 M to 0.15 M sodium phosphate, *p*H 6.88. Aliquots (0.1 ml.) of column fractions (20 ml.) were precipitated by the addition of H_2O (0.1 ml.) and ethanol containing 20% potassium acetate, *p*H 5.0 (0.5 ml.). The precipitate was collected by centrifugation, dissolved in H_2O (0.025 ml.) and assayed as described in the legend to Fig. 1.

The ultraviolet absorption spectrum of tRNA$_{\rm I}^{\rm Gly}$ contained the intense absorption at 335 nm which is characteristic of tRNAs containing 4-thiouridine; but this absorption formed part of the leading edge of the main peak at 260 nm and no clear peak could be resolved in a variety of solvents. The absence of a distinct peak at 335 nm is unusual, and it may be that partially oxidized species of tRNA$_{\rm I}^{\rm Gly}$ are contaminating the sample. We confirmed that the absorption at 335 nm was due to a thio-nucleotide by treating tRNA$_{\rm I}^{\rm Gly}$ with cyanogen

Table 2 Utilization of ^{14}C-Glycyl-tRNA$^{\rm Gly}$ Species for Protein Synthesis

Messenger	^{14}C-Glycyl-tRNA$^{\rm Gly}$ (total c.p.m. added)	Radioactivity incorporated into protein (%)
f2	tRNA$_{\rm I}^{\rm Gly}$ (5,000)	197 (2)*
T4		114 (2)
f2	tRNA$_{\rm IIA}^{\rm Gly}$ (4,500)	1,580 (35)
T4		1,155 (26)
f2	tRNA$_{\rm IIB}^{\rm Gly}$ (6,000)	2,701 (45)
T4		1,472 (25)
f2	tRNA$_{\rm III}^{\rm Gly}$ (5,400)	2,620 (49)
T4		1,481 (27)

Assay of incorporation into protein was carried out as described by Lodish[11] except using a modified ribosome preparation[12].

* This level of incorporation is of the same order as the blank which has already been subtracted.

Table 3 Trinucleotide Dependent Binding of ^{14}C-Glycyl-tRNA$^{\rm Gly}$ Species to *E. coli* Ribosomes

		Radioactivity bound (c.p.m.)			
^{14}C-Glycyl-tRNA$^{\rm Gly}$	No triplet	GGG	GGA	GGU	GGC
tRNA$_{\rm I}^{\rm Gly}$	45	42	44	49	40
tRNA$_{\rm IIA}^{\rm Gly}$	76	312	234	172	96
tRNA$_{\rm IIB}^{\rm Gly}$	74	270	238	174	76
tRNA$_{\rm III}^{\rm Gly}$	283	248	251	677	726

Reaction conditions were as described by Nirenberg and Leder[13], except that 0.04 M $MgCl_2$ was used. We thank Dr John Carbon for the samples of the trinucleotides.

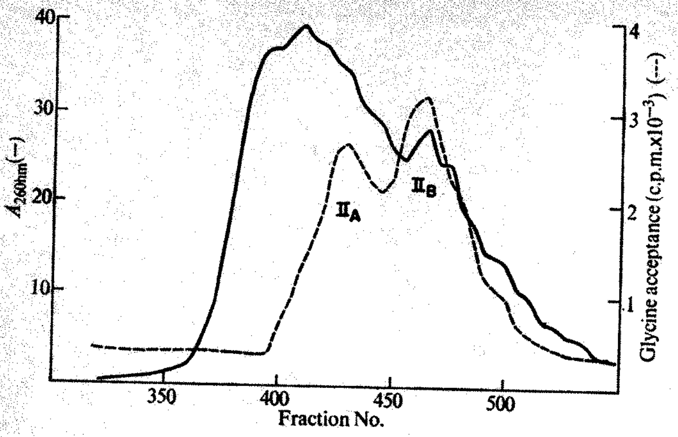

Fig. 3 Rechromatography of crude $\text{tRNA}_{\text{II}}^{\text{Gly}}$ on DEAE-cellulose. Fractions enriched in $\text{tRNA}_{\text{II}}^{\text{Gly}}$ (Fig. 1) (160,000 A_{260} units) were made 0.05 M in sodium acetate, *p*H 5.0, and applied to a column (100 × 6 cm) of DEAE-cellulose, equilibrated with buffer (0.02 M sodium acetate, *p*H 5.0, 0.01 M $MgCl_2$, 0.005 M $Na_2S_2O_3$, 0.001 M EDTA). Elution was carried out with 16 l. of a linear gradient from 0.35 M to 0.55 M NaCl in the same buffer. Aliquots (0.025 ml.) of column fractions (20 ml.) were assayed as described in the legend to Fig. 1.

bromide[17,18] which resulted in complete loss of absorption at 335 nm. This reaction specifically removes sulphur from thio-nucleotides[17,18].

Table 4 Base Analysis of $\text{tRNA}_{\text{I}}^{\text{Gly}}$

	Uridine	Guanosine	Adenine	Cytidine	4-Thiouridine
		(nmol per A_{260} of $\text{tRNA}_{\text{I}}^{\text{Gly}}$)			
Analysis 1	28.9	27.0	27.2	27.8	0.9
Analysis 2	28.5	25.6	27.1	28.2	0.8
Average	28.7	26.3	27.1	28.0	0.85
Composition (residues per mol)	22.1	20.2	20.9	21.5	0.65 (1)

The analytical conditions were as described by Uziel, Koh and Cohn[14]. The composition was calculated from the glycine acceptance value of 1,300 pmol per A_{260} unit.

The absence of minor bases, with the exception of 4-thiouridine, in $\text{tRNA}_{\text{I}}^{\text{Gly}}$ raises several interesting questions. Its failure to participate in protein synthesis or to bind to ribosomes may reflect the absence of an essential minor base. For example, the common sequence G T ψ C must be missing, and although a tRNA missing ribothymidylic acid is known to function in protein synthesis[19], there is some evidence that this sequence is essential for proper binding to ribosomes[20]. But the tRNA is recognized by the glycyl-tRNA synthetase. A single glycyl-tRNA synthetase has been found in *S. aureus*[21], and a single synthetase is also present in *S. epidermidis*. Clearly, minor bases (with the possible exception of 4-thiouridine) are unimportant in this respect. This observation agrees with the suggestion that the stem region of certain tRNAs is involved in recognition by the aminoacyl synthetase[22]. This region is devoid of minor bases in the tRNAs which have been sequenced so far.

Function of $\text{tRNA}_{\text{I}}^{\text{Gly}}$

The presence in both *S. aureus* and *S. epidermidis* of tRNAs which do not function in protein synthesis makes it unlikely that these are artefacts. Furthermore, they occur in normal quantities and reproducible amounts—in both organisms $\text{tRNA}_{\text{I}}^{\text{Gly}}$ represents about 40% of the total tRNA^{Gly}. This species may be a precursor of one or more of the other tRNA^{Gly} species in which the sole modification has been the conversion of a uridine residue to 4-thiouridine. To account for the absence of further modification, it is then necessary to postulate that this tRNA is sequestered in some manner for use in peptidoglycan synthesis. Alternatively, the 4-thiouridine residue may be located abnormally and might serve to protect the molecule from the other modifying enzymes. Finally, it is possible that $\text{tRNA}_{\text{I}}^{\text{Gly}}$ represents a unique gene product with a discrete function in peptidoglycan synthesis. In this case, it must lack the necessary recognition sequences for the usual modifying enzymes (such as methylases). Its function in peptidoglycan synthesis would then result from its availability over other species of tRNA^{Gly}, which would be engaged in protein synthesis.

The bridge amino-acids, glycine and serine in *S. epidermidis*, occur in the peptidoglycan in an amount which is at least equal to the total amount of these amino-acids present in all of the cell protein[23]. This occurs because the cell wall represents approximately 25% of the dry weight of the organism. It therefore seems reasonable that the bacterial cell has evolved a mechanism which ensures an adequate supply of these amino-acids for cell wall synthesis, and specifically in a form in which they cannot be used for protein synthesis.

That all four isoaccepting species of tRNA^{Gly} work equally well in the *in vitro* assay for peptidoglycan synthesis seems to indicate a certain lack of specificity. But the possible origin of $\text{tRNA}_{\text{I}}^{\text{Gly}}$ suggests an explanation for this phenomenon. Originally, only tRNA^{Gly} species functional in protein synthesis would be present in the cell and competition would be necessary to utilize glycyl-tRNA^{Gly} for peptidoglycan synthesis. The "modification" of an existing species of tRNA^{Gly}, such that it no longer functioned in protein synthesis but still functioned in peptidoglycan synthesis, might then yield a selective advantage. No further advantage would be gained by losing the ability to utilize the other species of tRNA^{Gly} for peptidoglycan synthesis.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Collapsed or Neutron Star Companions of Bright Stars

Cameron[1] and Stothers[2] have suggested that the companion to ε Aurigae is a collapsed star. Epsilon Aurigae is one of several binary stars with large mass functions and invisible secondaries and so far the primaries of two of the brightest of these, ν Sgr (ref. 3) and β Lyrae, have been found to have helium-rich atmospheres. This shows that mass exchange has occurred, and that the visible star has been stripped down to its hydrogen deficient core by transferring matter into the vicinity of the former secondary. This explanation for ε Aur is the third of four possibilities discussed by Stothers. The proof of it would be the discovery of anomalously strong He I lines, such as $\lambda 5876$, which appear in cool helium rich stars like R Cr B (ref. 4). This spectroscopic check should be made.

Huang suggested an explanation for the low luminosity of the apparently more massive component of these systems when he showed that the geometrical eclipse of β Lyrae was consistent with the faint massive star being disk shaped (though with some central condensation[5]). I pointed out[6] that the reduced central pressure of a disk compared with a sphere would result in a lower luminosity. On a time scale imposed by transport of angular momentum inside the disk and to the circumstellar shell, the massive star would become more circular and luminous, eventually evolving into a system like V356 Sgr in which both components are visible. The problems of the secular stability of disk shaped stars are not well understood, but there is no good theoretical basis for denying their existence.

In a system which has undergone mass exchange, the star that is expected to collapse first through fuel exhaustion is the lower mass star, the primary. It is more luminous, less massive, and only has helium to burn, whereas the other star is an almost zero age, normal composition star. The relative amounts of fuel available for the two stars, and the anomalous luminosities of the two components, ensure that the star which is visible for the time being will burn out in a small proportion of the main sequence lifetime of the disk star which is becoming visible.

If there are two or three stars brighter than fourth magnitude in this anomalous state, there should be about 100 bright stars in the more advanced state in which the primary has burned out; the new primary should be about the same luminosity as the old. The visible component will usually be an O or B star near the main sequence. This number of bright O or B stars is remarkably similar to the total number known. It is certainly consistent with half the known B star binaries being relatively young, and the other half having their secondaries fully evolved. Because a high proportion of B stars are known to be binaries, it is possible, but somewhat less likely, that these evolved systems are B stars which now appear to be single.

There are arguments that the present primaries of these binary systems will be very inefficient at shedding more mass. Mechanisms known to be effective seem to depend on the presence of an outer hydrogen zone, either to provide a jump in molecular weight that extends the outer layers of the star, or to provide a shell source of energy. It seems that, with the hydrogen gone, the fate of these components will be implosion either to give a neutron star or a collapsed object. It would be useful if a selected group of the brightest B stars could be examined for pulsars at the same coordinates in order to examine these possibilities. A study of some of the nearest B stars by lunar occultation to discover whether the secondary component of single line binaries is indeed a visible star would also be of great interest. Close binary stars provide remarkably detailed information on the history and nature of their components. Full advantage of this fact should be taken in exploring the newer more exotic areas of astrophysics.

The evidence from infrared observations discussed by Cameron and Stothers might in principle be used to disentangle the radiation of the secondary from that of circumstellar gas and dust. Attempts to do this have so far been hampered by lack of understanding of the range of phenomena in single stars. Confusion has been added by the systematic errors of some of the earlier observations and the problems of disentangling these from genuine time variations of objects[7]. Observations of some of the binaries are reported in a tabulation of photometric observations[8]. The infrared studies are continuing but the other approaches suggested above may increase the rate of progress in the search for the physical properties of neutron stars and collapsed stars.

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Observed Abundance Distribution of Chemical Elements as a Test of Alfvén's Theory of the Origin of the Solar System

MAGNETIC fields act on the orbits of ions and Alfvén[1] suggested many years ago that this effect was important during the early history of the solar system. Neutral atoms and ions will follow different paths which may cause a separation effect. In the work described here, the ionization energy has been used as a parameter and the abundances of the chemical elements in ordinary chondrites, terrestrial magma and lunar rocks have been compared with solar abundances.

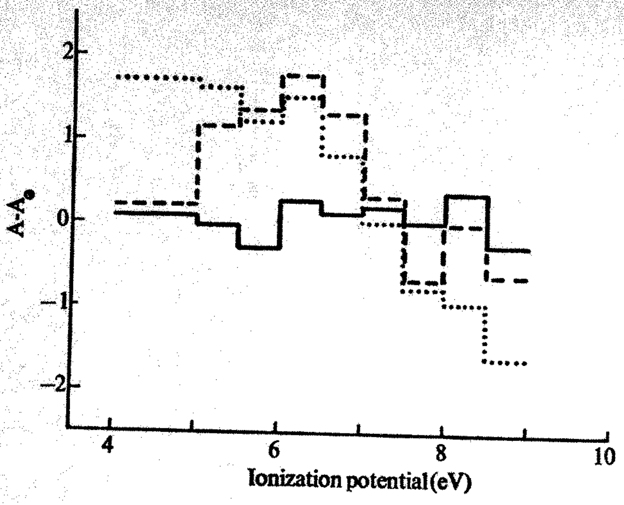

Fig. 1 The chemical abundances of the elements in ordinary chondrites (——), terrestrial magma (. . .) and lunar rocks (- - -) relative to the solar values versus the ionization potential of the element. The ordinate is a logarithmic scale.

As the Sun contains nearly all the mass in the solar system there is good reason to believe that the solar abundances reflect the primordial chemical composition of the solar system. But this is not true for a few of the elements which are involved in solar energy production and for elements such as Li, Be and B which are destroyed at existing temperatures near the bottom of the solar convection zone. Such elements have been excluded from the comparison.

My work has been based on abundance data from several sources. Wedepohl[2] has compiled the abundances in ordinary chondrites and in terrestrial magmatic rocks. The latter is an average of different types of rocks, taking into account the terrestrial distribution of each type, thus representing the average chemical composition of the upper terrestrial magma. I have used the average value of the abundance data published by Morrison *et al.*[3] for seven lunar rocks from the Apollo 11 mission. Except for a few elements, the chemical compositions of the different rock samples are nearly the same. Hauge and Engvold[4] have compiled solar abundance data. For some elements, there are still discrepancies in the solar abundances as derived by different methods, but for the comparison reported here the uncertainty in the solar abundances is of minor importance.

In this communication the abundance of elements in ordinary chondrites, terrestrial magma and lunar rocks is given relative to the solar value for each element. The solar abundances are adjusted in scale such that on average they come close to the abundances in the other objects.

Ordinary chondrites, terrestrial magma and lunar rocks have been investigated as follows: the relative abundances for all elements within a certain ionization potential interval and the average values of their logarithms[4] have been derived. The number of elements within each interval varies from two to nine. All elements were given the same reliability weight. A histogram of the relative abundances versus ionization potential is shown in Fig. 1.

The available abundance data do not necessarily represent the mean abundance of the object. The terrestrial core, for example, has a high iron content; the iron abundance I have used is 3.54% of the total mass. If, however, this value is increased by a factor of ten, the histogram level in Fig. 1, between 7.5 and 8 eV, should be 0.125 dex higher. Such a change does not alter the general trend of the diagram. When each element is plotted in the diagram, there is considerable scatter of the points, but about 90% of the elements are within the relative abundance range of 0.1 to 10 of the average value. By using many trace elements, representative mean values should be obtained.

The histograms based on forty-four elements show clear trends. In the case of terrestrial magma and lunar rocks, the step curve falls off toward higher ionization potentials corresponding to relative abundance depletions of 10^{-2} to 10^{-3}. For the elements with low ionization potentials the terrestrial abundance exceeds that of lunar rocks by a factor of 30. These results support Alfvén's[1] ideas about the formation of the Moon and the Earth.

The chondrite abundances seem to be independent of the ionization potential, and chondrites may reflect the composition of the original matter. As mentioned previously, with some exceptions, we should expect to find this composition on the Sun. The chondrite histogram in Fig. 1 shows a depression at 5–6 eV. This depletion can easily be explained by erroneous determination of the solar abundances of In and rare earth elements. At higher ionization potentials, the solar abundances of Cd, W, Os and Ir may be doubtful. I suspect that the chemical abundances in chondrites are even closer to the "true" solar values, and hence to the primordial matter, than Fig. 1 suggests. Because the chemical composition of chondrites is known, we can compare the lunar and terrestrial data with the chondrite values (Fig. 2). The histogram curves for the relative lunar and terrestrial abundances now become smoother, and there is a systematic trend between lunar and terrestrial data which may be significant. Above 5.5 eV the terrestrial abundances are depleted compared with the lunar abundances, while for lower ionization potentials the opposite situation obtains.

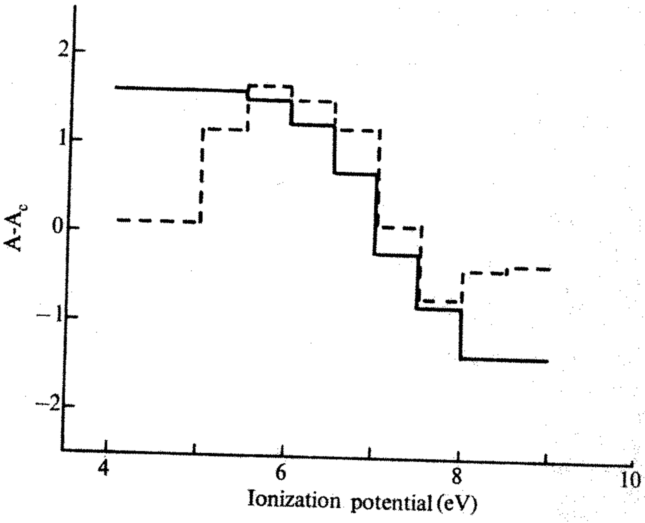

Fig. 2 The chemical composition in terrestrial magma (——) and lunar rocks (- - -) as a function of the ionization potential. Abundances are given relative to that of ordinary chondrites.

The investigations reported here lead to the following tentative conclusions. Ionized matter in magnetic fields played an important part in the formation of the Earth and the Moon, which were formed in different ionization conditions.

I shall assume that the energy which caused the ionization increases towards the Sun. Then the Moon must have been formed on the inner side of the Earth. This assumption is also supported by the high density of Mercury which may be due to a higher iron content, while the less dense planet Mars should be overabundant on elements with low ionization potentials such as Na, Al, K and Ca.

Considering the ionization potentials only, I cannot give a complete answer to these questions. Many other physical and chemical properties of matter must be taken into account in a theory for the solar system.

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Pyrolitic Graphite Microcalorimeter for the Measurement of X-Ray Absorbed Dose

To meet the need for absolute standards of absorbed dose for X-rays, the National Physical Laboratory together with other national laboratories is investigating methods based on microcalorimetry. The ideal would be to measure "local" absorbed dose in materials such as soft tissue to which water would represent a fairly satisfactory approximation. However, as Report 14 of the International Commission on Radiation Units and Measurements[1] states, "the direct determination of the absorbed dose at a point in a liquid (for example, water) has not been feasible primarily because of difficulties of achieving homogeneity of the irradiated system". An indirect method, in which the absorbed dose is determined in a solid "reference" material, is thus at present used.

The choice of a reference material is severely restricted by the desirability of avoiding not only endothermic and exothermic reactions but also significant energy storage (as, for example, by lattice deformation) and materials of high atomic number (which give rise to difficulties in deriving the absorbed dose in a material of low effective atomic number such as water). Thus[1] polystyrene and carbon (as graphite) "are presently considered to be the most suitable materials for absorbed dose calorimetry". Of these materials, carbon would be the obvious choice as a pure elemental substance were it not for the disadvantage that its electrical resistivity ($\sim 10^{-3}$ Ωcm as ordinary graphite) is too small for it to be used for calibration purposes by means of Joule self-heating, and because of reservations[1] about possible reactions induced by radiation associated with persistent gas adsorption. We believe that both these objections may be overcome by the use of pyrolytic graphite. Gas adsorption in this form of graphite, which is virtually impermeable, is negligible in comparison with ordinary graphite, while the marked anisotropic electrical properties can be exploited to achieve calibration self-heating.

Microcalorimeters of the "local" absorbed dose type are usually calibrated by comparing the temperature rise resulting from irradiation in a thermally isolated portion of the chosen material (the "absorber") with the temperature rise produced by a known amount of electrical energy dissipated in a small heater winding either embedded in or attached to the absorber. This procedure needs careful scrutiny for the possible effects of temperature gradients and accompanying thermal transients present in the case of electrical heating (owing to the discrete nature of the heating source), but largely absent during the "through-the-bulk" heating by X-ray irradiation. Laughlin and Genna[2] have stressed this need to consider carefully such effects, Petree and Lamperti[3] have discussed methods of correcting for them and Domen[4] has described a method of minimizing them by means of what he terms a "heat loss compensated" calorimeter. It has previously been assumed that inhomogeneous calibration heating is unavoidable in the case of a material such as ordinary graphite since (unlike plastic materials loaded with a small amount of carbon to make them partially conducting) its resistivity is so low that it is "not suitable for use as [its own]—heating resistor" (ref. 1). Nevertheless, "through-the-bulk" heating during calibration is clearly very desirable.

Table 1 Physical Properties of Pyrolytic Graphite

Density	2.2 g/cm^3
Purity	Metallic impurities typically 10 p.p.m.
Specific heat	$\sim$0.7 J/g deg. C
a direction thermal conductivity	$\sim$3.8 J cm/cm^{2}s deg. C
c direction thermal conductivity	$\sim$0.025 J cm/cm^{2}s deg. C
a direction electrical resistivity	$\sim 400 \times 10^{-6}$ Ωcm
c direction electrical resistivity	$\sim$0.7 Ωcm
a direction emissivity	0.8 to 0.9
c direction emissivity	0.5

To permit carbon to be used as the calorimetric material as its own electrical resistor, we are investigating the use of pyrolytic graphite. This material is a pure polycrystalline form of graphite exhibiting a high degree of preferred orientation, and in consequence it has marked electrical and thermal anisotropy, the electrical and thermal conductivities in the *c* direction being orders of magnitude less than the corresponding quantities in an *a* direction (the latter being any direction at right angles to the *c* direction). Details of the method of production and structure of pyrolytic graphite have been well summarized[5-8]. Table 1 sets out typical values of the physical properties of "as-deposited" pyrolytic graphite of special interest in the present context. We are investigating these properties, more especially the degree of uniformity both of density and of resistivity in the *c* direction, the latter being the quantity which it is hoped to exploit for electrical self-heating. We are also investigating the problems associated with machining the material with sufficient precision without significantly disturbing resistivity in the *c* direction. An "absorber" of pyrolytic graphite of the dimensions commonly used in a microcalorimeter can be arranged to have a resistance of several ohms which, although not low enough to create serious difficulties, is sufficiently low to raise questions about the fabrication of suitable electrode surfaces and also the mode of attachment of electrical connexions, to which we are also giving attention. Further, we have concerned ourselves with the possible effects of prolonged exposure to high energy photons on, for example, resistivity in the *c* direction. We are also investigating possible anisotropy of interaction with X-rays.

A comprehensive theoretical study of the application of pyrolytic graphite in a "local" absorbed dose microcalorimeter has been completed which has led to a prototype design, now under construction. The exploitation of the *c* direction resistivity to provide Joule self-heating for calibration purposes promises a considerable simplification in the design and use of a multi-jacketed adiabatic or quasi-adiabatic system; for example, the usual servo-heating system for the "jacket" can be eliminated. Again, the thermal anisotropy of the material can be exploited in the practical layout of the calorimeter, while the fact that pyrolytic graphite is virtually impermeable will enable it to be used as the vacuum jacket if so desired. We plan to operate the calorimeter on a basis in which irradiation and calibration heating go on simultaneously.

The proving of pyrolytic graphite as a suitable calorimetric reference material will contribute to the establishment of an absorbed dose standard for the United Kingdom, while the eventual intercomparison of such a standard with other standards should contribute to our knowledge of the nature and magnitude of the systematic errors in this field.

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Convection Plumes in the Lower Mantle

THE concept of crustal plate motion over mantle hotspots has been advanced[1] to explain the origin of the Hawaiian and other island chains and the origin of the Walvis, Iceland–Farroe and other aseismic ridges. More recently the pattern of the aseismic ridges has been used in formulating continental reconstructions[2]. I have shown[3] that the Hawaiian–Emperor, Tuamotu–Line and Austral–Gilbert–Marshall island chains can be generated by the motion of a rigid Pacific plate rotating over three fixed hotspots. The motion deduced for the Pacific plate agrees with the palaeomagnetic studies of seamounts[4]. It has also been found that the relative plate motions deduced from fault strikes and spreading rates agree with the concept of rigid plates moving over fixed hotspots. Fig. 1 shows the absolute motion of the plates over the mantle, a synthesis which satisfies the relative motion data and quite accurately predicts the trends of the island chains and aseismic ridges away from hotspots.

I now propose that these hotspots are manifestations of convection in the lower mantle which provides the motive force for continental drift. In my model there are about twenty deep mantle plumes bringing heat and relatively primordial material up to the asthenosphere and horizontal currents in the asthenosphere flow radially away from each of these plumes. The points of upwelling will have unique petrological and kinematic properties but I assume that there are no corresponding unique points of downwelling, the return flow being uniformly distributed throughout the mantle. Elsasser has argued privately that highly unstable fluids would yield a thunderhead pattern of flow rather than the roll or convection cell pattern calculated from linear viscous equations. The currents in the asthenosphere spreading radially away from each upwelling will produce stresses on the bottoms of the lithospheric plates which, together with the stresses generated by the plate to plate interactions at rises, faults and trenches, will determine the direction in which each plate moves.

Evidently the interactions between plates are important in determining the net force on a plate, for the existing rises, faults and trenches have a self-perpetuating tendency. The plates are apparently quite tough and resistant to major changes, because rise crests do not commonly die out and jump to new locations and points of deep upwelling do not always coincide with ridge crests. (For example, the Galapagos and Réunion upwellings are near triple junctions in the Pacific and Indian Oceans. Asthenosphere motion radially away from these hotspots would help to drive the plates from the triple junctions, but there is considerable displacement between the "pipes to the deep mantle" and the lines of weakness in the lithosphere which enable the plates to move apart.) Also, a large isolated hotspot such as Hawaii can exist without splitting a plate in two. I believe it is possible to construct a simple dynamic model of plate motion by making assumptions about the magnitude of the flow away from each hotspot and assumptions about the stress/strain rate relations at rises, faults and trenches. Such a model has many possibilities to account for past plate motions; hotspots may come and go and plate migration may radically change the plate to plate interactions. But the hotspots would leave visible markers of their past activity on the seafloor and on continents.

This model is compatible with the observation that there is a difference between oceanic island and oceanic ridge basalts[5,6]. It suggests a definite chain of events to form the island type basalt found on Hawaii and parts of Iceland. Relatively primordial material from deep in the mantle rises adiabatically up to asthenosphere depths. This partially fractionates into a liquid and solid residual, the liquid rising through vents to form the tholeiitic part of the island. The latter alkaline "cap rocks" would be generated in the lithosphere vent after plate motion had displaced the vent from the "pipe to the deep

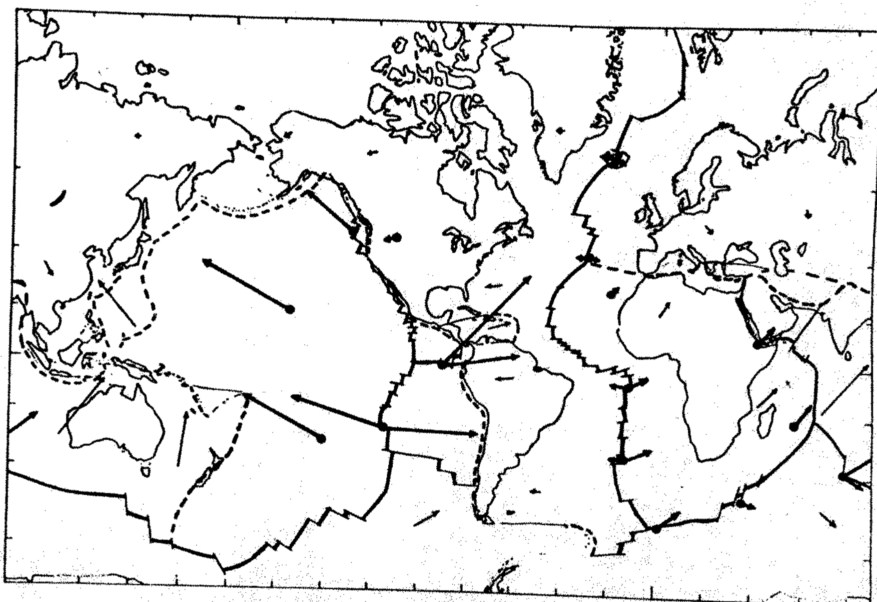

Fig. 1 The arrows show the direction and speed of the plates over the mantle; the heavier arrows show the plate motion at hotspots. This synthesis was based on relative plate motion data (fault strikes and spreading rates) and predicts the directions of the aseismic ridges/island chains emanating from the hotspots.

mantle". In contrast, the ridge basalts would come entirely from the asthenosphere, passively rising to fill the void created as plates are pulled apart by the stresses acting on them. The differences in potassium and in rare earth pattern for island type and ridge type basalts may be explained by this model. Moreover, the 2 billion year "holding age" advocated by Gast[7] to explain lead isotope data of Gough, Tristan da Cunha, St Helena and Ascension Islands may reflect how long the material was stored in the lower mantle without change prior to the hotspot activity.

My claim that the hotspots provide the driving force for plate motions is based on the following observations to be discussed below. (1) Almost all of the hotspots are near rise crests and there is a hotspot near each of the ridge triple junctions, agreeing with the notion that asthenosphere currents are pushing the plates away from the rises. (2) There is evidence that hotspots become active before continents split apart. (3) The gravity pattern and regionally high topography around each hotspot suggest that more than just surface volcanism is involved at each hotspot. (4) Neither rises nor trenches seem capable of driving the plates.

The symmetric magnetic pattern and the "mid-ocean" position of the rises indicate that the rises are passive. If two plates are pulled apart, they split along some line of weakness and in response asthenosphere rises to fill the void. With further pulling of the plates, the laws of heat conduction and the temperature dependence of strength dictate that future cracks appear down the centre of the previous "dike" injection. If the two plates are displaced equally in opposite directions or if only one plate is moved and the other held fixed, perfect symmetry of the magnetic pattern will be generated. The axis of the ridge must be free to migrate (as shown by the near closure of rises around Africa and Antarctica). If the "dikes" on the ridge axis are required to push the plates apart, it is not clear how the symmetric character of the rises could be maintained. The best argument against the sinking lithospheric plates providing the main motive force is that small trench-bounded plates such as the Cocos plate do not move faster than the large Pacific plate[8]. Also, the slow compressive systems would not appear to have the ability to pull other plates away from other units. The pull of the sinking plate is needed to explain the gravity minimum and topographic deep locally associated with the trench system[9], but I do not wish to invoke this pull as the principal tectonic stress. This leaves sub-lithospheric currents in the mantle and the question now is: are these currents great rolls (mirrors of the rise and trench systems), or are they localized upwellings (that is, hotspots)?

A recent world gravity map[10] computed for spherical harmonics up to order 16 shows isolated gravity highs over Iceland, Hawaii, and most of the other hotspots. Such gravity highs are symptomatic of rising currents in the mantle. Even if the gravity measurements are inaccurate (different authors have very different gravity maps), the fact remains that the hotspots are associated with abnormally shallow parts of the oceans. For example, note the depth of the million square kilometres surrounding the Iceland, Juan de Fua, Galapagos, and Prince Edward hotspots. The magnitude of the gravity and topographic effect should measure the size of the mantle flow at each hotspot.

There is evidence of continental expression of hotspot activity in the lands bordering the Atlantic: the Jurassic volcanics in Patagonia (formed by the present day Bouvet Island plume), the ring dike complex of South-west Africa and flood basalts in the Parana Basin (Tristan da Cunha plume), the White Mountain Magma series in New Hampshire (the same hotspot that made the New England Seamount Chain (Azores plume?)), the Skaegaard and the Scottish Tertiary Volcanic Province (Iceland plume) and perhaps others. I claim this line-up of hotspots produced currents in the asthenosphere which caused the continental break-up leading to the formation of the Atlantic. Likewise the Deccan Traps (Reunion plume) were symptomatic of the forthcoming Indian Ocean rifting. A search should be made for such continental activity, particularly in East Africa and the western United States (the Snake River basalts?) as an explanation for the rift features found there. There is a paucity of continental hotspots in Fig. 1; perhaps this is a bias due to continental complexity versus oceanic simplicity, but the model presented here predicts that most hotspots will be near a spreading rise.

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Fossil Pingos in the South of Ireland

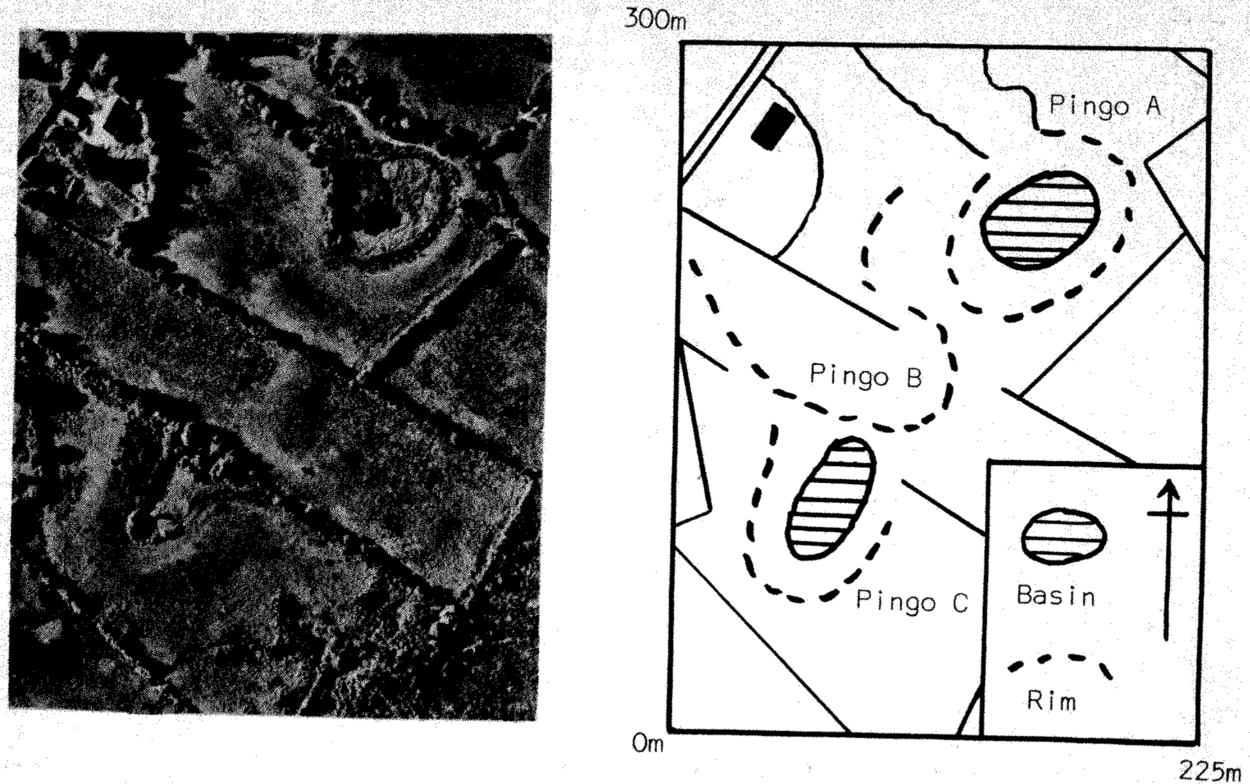
REMAINS of former pingos or ice-lens mounds are known in the Low Countries, Scandinavia, East Anglia[1] and Wales[2]. They are also widely distributed in the south of Ireland.

Fine examples occur near Camaross, on the road from Wexford to New Ross, 9 km west-north-west of Wexford town. A cluster of at least twenty fossil pingos north-east of Camaross Cross Roads (S891249) have been specially photographed by Dr J. K. St Joseph, Director in Aerial Photography, University of Cambridge (obliques 23/890245 and 7; verticals K17/W25–30). Part of K17/W26 is reproduced here by kind permission (Fig. 1*a*).

Three fossil pingos are seen. Pingo A (top right) has a basin about 60 m in diameter; the enclosing rim, which is almost complete, rises in a grassy ridge 1.5 m above the surrounding badly drained rushy ground (well seen on the south-east side). The elongated basin of pingo B does not contain open water, but the rushy vegetation inside the rim and outside it on the south-east is in contrast with the grass cover of the rim. Pingo C (bottom left) has an elongated basin which contains a wet swamp. In this vicinity, ridges of rock at about 75 m OD (ordinance datum) separate small valleys whose lower slopes (falling from north-west to south-east) are covered by soliflucted till with very poor natural drainage. The pingos formed near the base of the slopes.

Fine examples also occur at 60 m OD in Carrigeenhill Townland (W945953) on the road from Fermoy to Tallow, 14 km east-south-east of Fermoy. Here there is a rock-ridge to the north of the road, and a small valley partly filled with badly drained soliflucted till to the south. A large field abutting against the south side of the road showed at least three pingo basins and several curved ridges. When seen, the field was in the course of being drained and the lay-out of the drainage ditches had been imposed by the distribution of the pingo basins and ridges, which had disturbed the solifluction slope.

About 5 km west-north-west of Castleisland, the road from Castleisland to Tralee runs through a series of groups of fossil



a *b*

Fig. 1 *a*, Vertical aerial photograph (Cambridge K17/W26; reproduced by kind permission) of three fossil pingos in Camaross Townland, Co. Wexford, Ireland. *b*, Outline map to accompany aerial photograph.

pingos at about 35 m OD. In Ballyegan Townland (Q962113) a small badly drained hollow is surrounded by outcrops of limestone; active quarrying is going on immediately to the west. There are at least three crescent shaped pingo ridges in the basin; one has an arc of 180° and a height of 1.5 m. In the adjoining Coolgarriv Townland (Q950117) there is a large marshy area, sloping gently to a flat valley bottom drained by the River Maine, with pingo features on both sides of the road. The road traverses one large pingo with appreciable rises where it crosses the rims which are about 100 m apart. South of the road, an almost continuous rim with an arc of 180° can be seen. In the next adjoining Maglass and Maglass East Townlands (Q945118) there are pingo features on both sides of the road.

These examples are only a few noted from main roads; many more will be revealed by survey. I will be obliged for information of other pingo features in Ireland. So far, all the examples noted lie south of the limit of the last glaciation.

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Determination of Hydrocarbons in Seawater Extracts of Crude Oil and Crude Oil Fractions

IN spite of very convincing evidence to the contrary, crude oil and oil products are still occasionally considered to be "insoluble" in aqueous systems. In view of recent reports of major ecological disruptions caused by oil pollution[1,2], it seemed imperative to collect more data on the solubility of oil and oil products in water systems[3,4]. We have isolated, identified and quantitatively determined major components present in seawater extracts of several crude oils and a kerosene.

Oil samples (25 ml.) were mixed with filtered seawater (1.5 l., Whatman No. 1 filter paper) in different ways to simulate natural process of contact between oil and water. Slow stirring (12 h) consisted of stirring with a magnetic stirrer (4 cm × 1 cm 'Teflon' coated) at a rate that produced an oil vortex which was never greater than 25% of the solution depth. Turbulent conditions were effected by rapid stirring (12 h) to produce contact between the oil and the stirring bar. All stirred samples were processed in glass stoppered bottles (2 l., 12 cm in diameter) equipped with bottom taps. Maximum mixing was accomplished by shaking the oil/water samples in an Erlenmeyer flask (2 l.) using the Burrell wrist action shaker. All experiments were conducted at 23° C. Processed samples were transferred carefully to separatory funnels (2 l.) and allowed to stand for 2 h before the two phases were separated. The aqueous phase was then extracted four times with doubly distilled pentane. The evaporated residue from the pentane extract was chromatographed on a Varian Aerograph-1200 gas chromatograph interfaced to a CEC-104 mass spectrometer[5]. Component structures were assigned on the basis of mass spectra, boiling point comparisons[6] and ultraviolet spectra. Concentration of dissolved compounds was determined by planimetry of gas chromatographic peaks.

Kuwait oil and a kerosene were stirred slowly, stirred turbulently and shaken with seawater. In general, slow stirring gave a reproducible aqueous extract that contained mostly aromatic (benzenes and naphthalenes in the low boiling range 80–262° C) compounds. As turbulence increased, however, more non-polar saturated hydrocarbons appeared in the seawater layer. Fig. 1 shows a gas chromatogram of the seawater extracts of Kuwait oil in conditions of slow

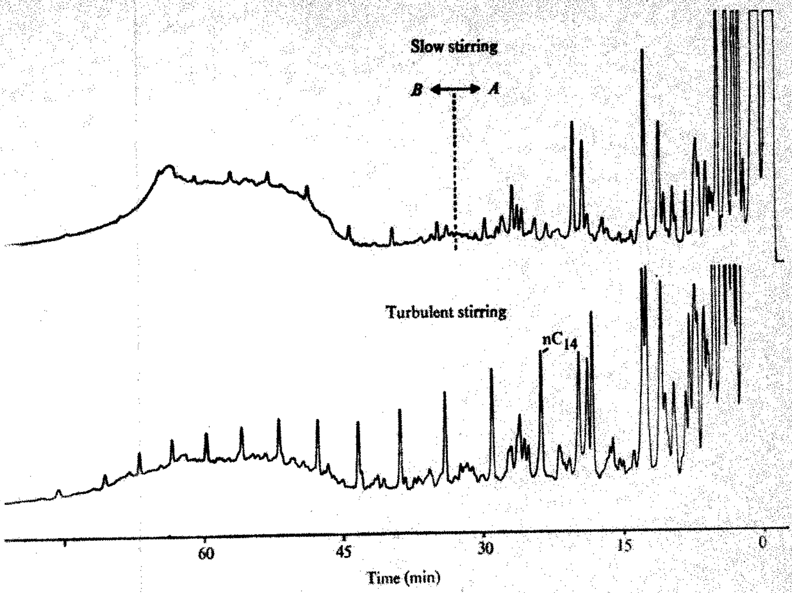


Fig. 1 Gas chromatograms of seawater extracts of Kuwait crude oil. Slow stirring conditions: *A*, benzene and naphthalene regions; *B*, polar aromatic region. Turbulent stirring conditions: increase in chromatogram complexity is due to presence of saturated hydrocarbons. The size of the column was 1/16 inch × 8 feet; the coating was 0.2% 'Apiezon L' on textured glass beads (80–100 mesh); temperature was 60°–220° C (4°/min); the carrier gas passed at 10 ml./min, and the chart speed was 15 inches/h.

and turbulent stirring. There was an increased concentration of saturated hydrocarbons in the aqueous extract when the mixture was stirred turbulently. The presence of saturated hydrocarbons in this extract was probably due to oil droplet suspension and not to true water solubility. Oil samples shaken with seawater produced a water phase (oil emulsion) with an oil content which was similar to that of the untreated oil.

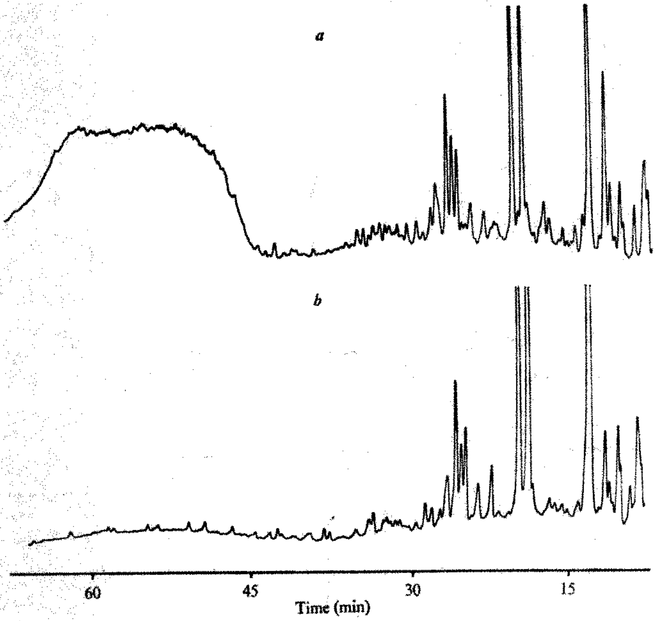


Fig. 2 Comparison of gas chromatograms of seawater extracts of Kuwait (*a*) and Louisiana (*b*) crude oil (slow stirring conditions). Specifications as in Fig. 1.

The high boiling envelope in Kuwait aqueous extract (Fig. 1*B*) is due mostly to polar aromatic material. This was established through gas chromatography of the aqueous extract on active silica gel. Polar solvents (25% CH_3OH/CH_2Cl_2) were needed to elute the bulk of this material. Fig. 2 compares the gas chromatogram of the Louisiana crude aqueous extract with that of the Kuwait extract. Although there are subtle differences in the naphthalene and benzene regions, the principal difference is in the intensity of the high boiling polar aromatic envelope.

The kerosene seawater extract (Fig. 3) contained a benzene and naphthalene distribution similar to the Kuwait extract, but concentrations of dissolved compounds varied markedly (Figs. 1 and 3; Tables 1 and 2). One of the peaks (No. 15, Fig. 3) is only found in significant amounts in the kerosene fraction and has been identified as biphenyl. The concentrations reported in Tables 1 and 2 represent the distributions of crude oil and oil fractions in seawater (equilibria conditions) and do not represent true solubilities of those compounds in seawater.

Methods are being sought for rapid identification of oil that will prove useful in the enforcement of oil pollution legislation. Gas chromatography of aqueous extracts of polluting oils provides an excellent, sensitive method for this purpose. In each oil or kerosene studied, significant differences in relative amounts of naphthalene compounds were observed (Fig. 4). Special attention should be drawn to relative isomer content, that is, 1 and 2-methyl naphthalenes and the 1 : 2, 1 : 6, 2 : 6-dimethyl naphthalenes of each sample. Because each isomeric aromatic compound has approximately

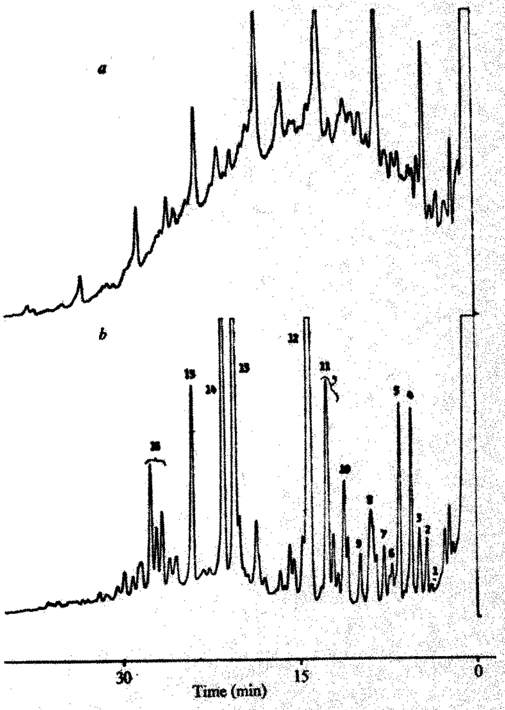
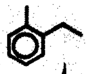
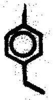
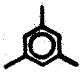
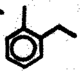
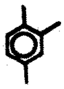
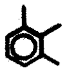
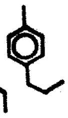
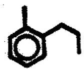
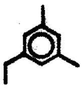
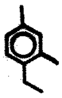
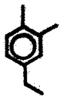
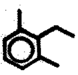
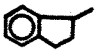
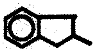
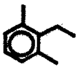
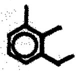
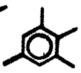
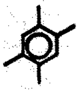
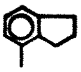
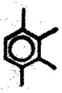
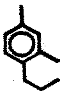
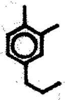
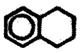
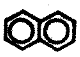
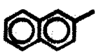
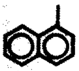
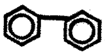
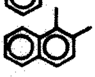
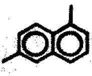
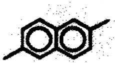


Fig. 3 Gas chromatograms of: *a*, kerosene; *b*, seawater extract of kerosene. Numbered peaks are identified and quantified in Table 1. Specifications as in Fig. 1.

Table 1 Substances isolated from Seawater Extract of Kerosene

COMPOUND		C B.PT.	PEAK #	CONC. (UG/L)
BENZENES				
1-METHYL-2-ETHYL BENZENE		161.3	2	6.68
1-METHYL-4-ETHYL BENZENE		161.99	2	
1:3:5-TRIMETHYL BENZENE		164.72	3	8.10
1-METHYL-2-ETHYL BENZENE		165.15	3	
1:2:4-TRIMETHYL BENZENE		169.35	4	20.15
1:2:3-TRIMETHYL BENZENE		176.08	5	18.07
			6	
1-METHYL-4-PROPYL BENZENE		183.30	7	5.93
1-METHYL-2-PROPYL BENZENE		184.80	7	
1:3-DIMETHYL-5-ETHYL BENZENE		183.58	7	
1:3-DIMETHYL-4-ETHYL BENZENE		188.20	8	18.17
1:2-DIMETHYL-4-ETHYL BENZENE		189.40	8	
1:3-DIMETHYL-2-ETHYL BENZENE		190.01	8	
1-METHYLINDANE		190.6	8	
2-METHYLINDANE		191.4	8	
1:3-DIMETHYL-2-ETHYL BENZENE		190.1	8	
1:2-DIMETHYL-3-ETHYL BENZENE		193.91	9	6.21
1:2:3:5-TETRAMETHYL BENZENE		198.00	10	16.57
1:2:4:5-TETRAMETHYL BENZENE		196.80	10	
4-METHYL INDANE		205.5	11	35.39
1:2:3:4-TETRAMETHYL BENZENE		205.04	11	
1:3-DIMETHYL-4-PROPYL BENZENE		206.6	11	
1:2-DIMETHYL-4-PROPYL BENZENE		208.5	11	
TETRAHYDRONAPTHALENE		207.57	11	
NAPTHALENES				
NAPTHALENE		217.96	12	152.89
2-METHYL NAPTHALENE		241.05	13	85.66
1-METHYL NAPTHALENE		244.64	14	63.43
BIPHENYL		255.2	15	27.49
1:2-DIMETHYL NAPTHALENE			16	32.95
1:6-DIMETHYL NAPTHALENE			16	
2:6-DIMETHYL NAPTHALENE		262	16	
TOTAL AROMATICS				610

the same physical property and is not easily attacked by bacteria, one would expect concentration ratios of isomeric groups to remain constant even after exposure to air or water. This technique is useful as long as aromatic constituents are still present in the contaminating oil. Specific compounds such as biphenyl (kerosene aqueous extract, Fig. 3, No. 15, and Fig. 4) will also aid in the identification of oil.

Petroleum and petroleum products are toxic to fish[7-9]. Unfortunately, the toxicity values reported are meaningless except as an initial screening estimate[10]. If we can assume that the relative lethal concentrations reported (Table 3) give a general idea of the toxicity index of oil and oil fractions in the polluted environments, then naphthalene and probably other naphthalene-type compounds are the most toxic components identified in the aqueous extracts. The greater toxicity of kerosene than Kuwait crude oil to fish is supported by the detection of much greater concentrations of naphthalene in the kerosene seawater extract (kerosene extract—159.9 μg/l., Kuwait crude extract—32.3 μg/l.). Thus by analysing seawater extracts it should be possible to establish a toxicity index of potential oil pollutants.

Changes in the behaviour of marine organisms, such as disruption in normal feeding sequences, sex attraction, host recognition in symbiotic relations and other intricate social interactions, may be caused by the presence of sublethal concentrations of soluble oil fractions. Because chemical communication among marine organisms is expected to be very susceptible to interferences by pollution, the effects of oil on such systems are being investigated in this laboratory.

The presence of a high boiling aromatic envelope (Fig. 1*B*, Table 2) in the aqueous extract of Kuwait oil is most interesting. Such water soluble materials, when concentrated and retained by marine animals[11], could present a health hazard. For this

Table 2 Relative Concentration of Aromatic Species in Kuwait Oil Seawater Extracts (Slow Stirring)

	μg/l.	Concentration
Benzenes and naphthalenes (Fig. 1*A*)	657	45.2%
Polar aromatics (Fig. 1*B*)	796	54.8%
Total amount of oil in water	1,453	
Concentration of individual compounds		
Naphthalene	32.3	(2.2%)
2-Methyl naphthalene	15.0	(1.0%)
1-Methyl naphthalene	18.0	(1.2%)

Table 3 Toxicity Data

Oil fraction	General toxicity range (mg/l.)	Specific toxicity data
(1) Crude oil	5,000	1–100 mg/l.—pronounced toxic effect on larval stages of crabs and shrimp
(2) Bunker C (No. 6 fuel oil)	2,400*	
(3) Diesel oil (No. 2 fuel oil)	200†	
(4) Kerosene (No. 1 fuel oil)	200†	
(5) Gasoline	90†	
(6) Benzene, toluene	10–90‡	386–1,180 mg/l. — mosquito fish (TLm—96 h)
(7) Naphthalene	4–5‡	1.8–3.2 mg/l.—fingerling salmon (death—72 h) 150 mg/l.—mosquito fish (TLm—96 h) 20–40 mg/l.—perch (death—1 h)
(8) Phenanthrene	4–5‡	
(9) Phenols	1–20‡	

These reported toxicity ranges have been determined under laboratory conditions and are not quantitatively valid for the natural environment.

TLm, Concentration at which 50% of the aquatic animals survive.
* Juvenile shad (TLm—48 h).
† Juvenile shad (TLm—24 h).
‡ Sunfish (death—1 h).

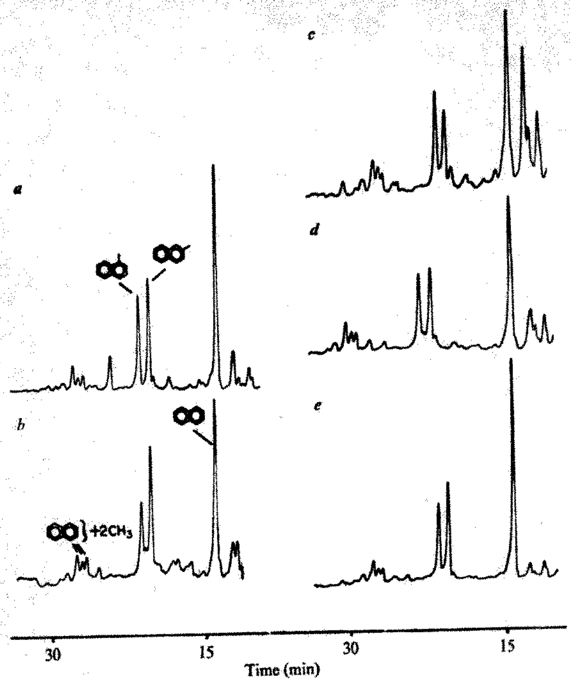


Fig. 4 Gas chromatograms of seawater extracts of: *a*, kerosene (Gulf grade); *b*, No. 6 fuel oils (North-East Petroleum Co.); *c*, Kuwait crude oil; *d*, La Rosa crude oil; *e*, Louisiana crude oil. Specifications as in Fig. 1.

reason, future investigations will concern the identification of water soluble components in the high boiling region.

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Stratospheric Warming observed by Nimbus 4

AN important feature of the winter stratosphere near the poles is the occurrence of "sudden warmings" where the temperature over a small area may rise by as much as 50 K in a few days, accompanied by a major change in circulation. Observation of these events, dependent on meteorological rocket and radiosonde ascents, has been hampered by the sparsity of data. Here we present data for a stratospheric warming obtained by the selective chopper radiometer on the Nimbus 4 satellite, which gives global coverage to considerably greater heights than has hitherto been possible.

The radiometer[1-3] has six channels, each accepting infrared radiation emitted by carbon dioxide in the atmosphere below the satellite at wavelengths of approximately 15 μm. The radiation measured by channel A originates in a layer approximately 20 km thick centred at the 2 mbar (42 km) level, while that measured by channel B originates in a layer of similar thickness centred at 20 mbar (26 km). Figs. 1*a* and *c* are northern hemisphere maps of channel A radiance, while Figs. 1*b* and *d* are northern hemisphere maps of channel B radiance. Such maps are produced routinely by 1500 h on the day following the day of the observations. A table is given of the black body temperature equivalent to infrared radiance for channels A and B. The interpretation in terms of atmospheric temperature is explained in ref. 3; as a rough guide it may be considered that these temperatures are those occurring in the region of the 2 mbar and 20 mbar levels respectively.

Figs. 1*a* and *b* show the situation on December 30, 1970. On channel A (Fig. 1*a*) a warm region with a maximum radiance of 95 mW m^{-2} sr^{-1} $(cm^{-1})^{-1}$ was developing at 45° N 65° E; 3 days earlier this warm region had been at 25° N 20° E with a maximum radiance of 85 mW m^{-2} sr^{-1} $(cm^{-1})^{-1}$. A corresponding warm region was present on channel B (Fig. 1*b*) with a maximum at 35° N 50° E, implying a northward tilt of the warm anomaly.

Table 1 Equivalent Temperature as a Function of Radiance for a Black Body

Radiance mW m^{-2} sr^{-1} $(cm^{-1})^{-1}$	Equivalent temperature (K)
30	201.0
40	213.7
50	224.7
60	234.5
70	243.6
80	251.9
90	259.8
100	267.2
110	274.2
120	281.0

By January 4, 1971, a great change had occurred in the temperature distributions observed by both channels. The warm area described above had intensified and at the 2 mbar level (Fig. 1*c*) had moved north to 70° N 90° E with a radiance at the centre of 120 mW m^{-2} sr^{-1} $(cm^{-1})^{-1}$. At this time the difference in equivalent temperature near the 2 mbar level between the hottest and coldest region was more than 60 K. The whole northern hemisphere was dominated by a wave number one pattern with little contribution from the higher wave numbers apparent on December 30. The pattern was similar at the 20 mbar level but the amplitude of wave number one was less and the phase is about 25° farther eastward. This implies a westward tilt of the warm anomaly of 1.5° longitude per km height. Subsequently the warm region increased little in intensity, but moved westward. On January 9, the warm region had moved to 75° N 40° E with a westward slope of 3° longitude km^{-1}; thereafter the warm region at the 2 mbar level moved farther westwards and decayed in intensity.

On channel A on December 30 (Fig. 1*a*), there was a warm region at 65° N 120° E and a corresponding warm region on channel B (Fig. 1*b*) at 65° N 170° E; this was what remained of a warming which had a maximum intensity on December 26 at 70° N 125° E at the 2 mbar level. On December 30 this warm anomaly had a westward tilt of 3° longitude km^{-1} while the cold anomaly over North America had a westward tilt of approximately 4.5° longitude km^{-1}. By January 2 this warm anomaly had disappeared from our maps.

The increase of amplitude of the warming and the westward phase tilt with height are to be expected if temperature varia-

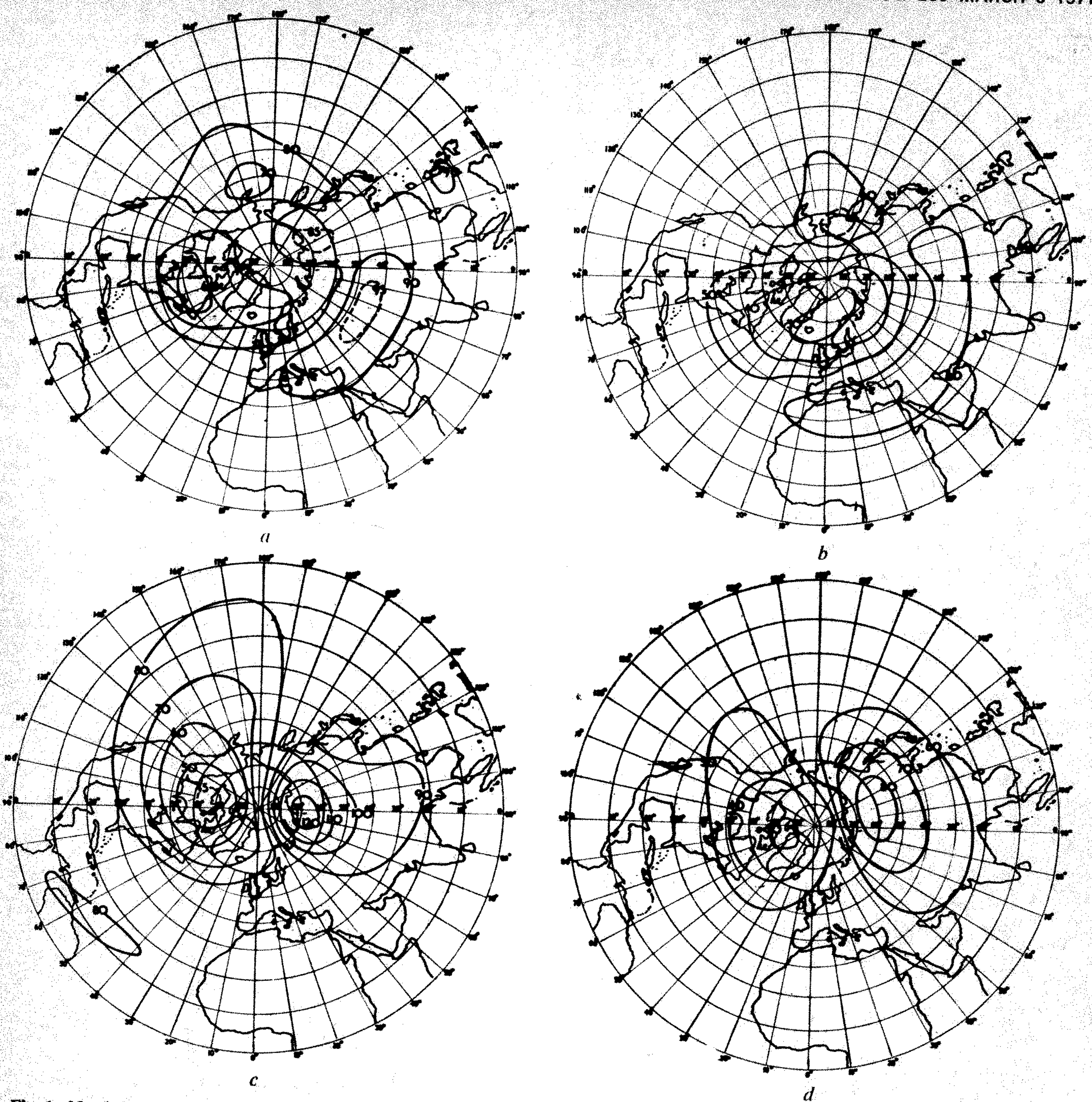

Fig. 1 North Polar stereographic maps showing isopleths of radiance mW m^{-2} sr^{-1} (cm^{-1})$^{-1}$ from channels A and B. The equivalent temperatures of a black body which would give the same radiance are given in Table 1. Each map was derived from data of 12 orbits extending to 80° N (ref. 3). *a*, Channel A (approximately 2 mbar), December 30, 1970; *b*, Channel B (approximately 20 mbar), December 30, 1970; *c*, Channel A, January 4, 1971; *d*, Channel B, January 4, 1971.

tions are caused by upward propagating planetary waves[4,5].

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BIOLOGICAL SCIENCES

Neonatally Induced Allograft Tolerance may be mediated by Serum-borne Factors

IN 1953, Billingham *et al.* discovered that mice inoculated neonatally with foreign lymphoid cells can often accept skin grafts from the same foreign strain, indicating that they have become "tolerant" to the alloantigens of the neonatally inoculated cells[1,2]. A similar tolerance can be induced in adult animals if they are rendered chimaeric by inoculation with foreign bone marrow after either whole body irradiation or treatment with immunosuppressive drugs[3,4].

Many explanations can be offered for the establishment and maintenance of allograft tolerance, but two hypotheses only will be considered here. According to the first, lymphoid cells that would have been reactive to a given set of antigens become permanently depleted or inactivated in a tolerant animal[5]. In the second hypothesis the reason why lymphoid cells from tolerant animals are not reactive *in vivo* is that they are temporarily suppressed by some factor which is present in the tissues or serum of the tolerant animals, for example, "tolerogenic" antigen or enhancing antibodies, which would act either on the lymphocytes or on the target cells.

We now report preliminary findings from a study using a cytotoxic test to ascertain whether mice neonatally made tolerant to allografts have lymphocyte-mediated immunity (detectable *in vitro*) against target cells of the strain to which they were tolerant *in vivo*, and whether serum from the tolerant animals can abolish such a manifestation of immunity.

Ten CBA and ten A mice were rendered tolerant by injecting within the first 24 hours after birth with 5 × 10^7 spleen cells of A × CBA F1 [2], tolerance being defined as the ability of approximately one month old mice to accept permanently skin grafts of A and CBA origin, respectively. Lymph nodes (axillary, inguinal, cervical and retroperitoneal) and serum were obtained from four 1–2 months old CBA mice which were tolerant to A, and from five A mice tolerant to CBA, each mouse being studied separately. The litter mates of these mice, which had also been injected with spleen cells neonatally, were shown to be tolerant by skin grafting tests; the mice used in the cytotoxic assays had not, however, received any skin grafts. Lymph nodes and serum from CBA and A mice which had not been injected with foreign cells were used as controls.

CBA and A fibroblasts derived from explanted adult lung tissue were plated *in vitro* and exposed to serum from specifically tolerant and control mice, after which lymph node cell (LNC) suspensions from the same mice were added. Instead of the colony inhibition technique, used previously[6], we used a modification of a similar test[7] in which the cytotoxic effect of immune lymphocytes is measured on all the cells in microcultures rather than on their ability to inhibit colony formation; smaller samples of lymphocytes and sera could therefore be used. Cultures of CBA and A fibroblasts, derived from the lungs of adult animals, were trypsinized, and 80–100 cells, suspended in Waymouth's culture medium containing 30% newborn calf serum, were seeded into each microwell of flat-bottomed 3040 Falcon Microtest II plates. On the next day the medium was removed and the sera to be tested were diluted 1 : 6 in Waymouth's medium and 0.1 ml. was added to each well, after which the plates were incubated for 45 min. The sera were then poured off, and LNC suspensions added, 0.2 ml. per well, each well receiving 400,000 LNC suspended in Eagle's minimum essential medium (MEM). The plates were incubated for an additional 45 min, and then 0.05 ml. of MEM containing 50% newborn calf serum was added to each well. The plates were covered with Falcon 3044 pressure-sensitive film, the lids were put on and the plates incubated at 37° C for 2–3 days on a Bellco rocker platform in an atmosphere of 5% CO_2 in air. The plates were then stained with crystal violet and the cells in each well counted, using coded material. Each determination was made on 8–11 wells treated identically.

The findings are presented in Table 1. It seems that LNC from

Table 1 Data from Cytotoxicity Tests with Explanted Lung Fibroblasts from CBA and A Mice, exposed to Lymph Node Cells (LNC) and Sera from Tolerant and from Control Animals

Experiment No.	Target cells	LNC	Serum	No. of cells per well (mean ± s.e.)	% Decrease in cell No./well with tolerant LNC and control as compared to tolerant serum
1-a	A	CBA tolerant	CBA tolerant	155.2 ± 6.4	
			CBA normal	117.9 ± 2.7 †	24.0
		CBA normal	CBA tolerant	152.3 ± 4.8	
			CBA normal	153.9 ± 7.0	
1-b	CBA	A tolerant	A tolerant	52.5 ± 3.2	
			A normal	33.8 ± 3.3 ‡	35.6
			—	28.3 ± 2.9	
		CBA normal	A normal	46.3 ± 4.2	
		CBA tolerant		36.5 ± 2.5	
2-a	A	CBA tolerant	CBA tolerant	34.5 ± 1.5	
			CBA normal	21.1 ± 1.2 ‡	38.8
			—	24.3 ± 1.9	
		A tolerant	—	32.4 ± 1.2	
		A normal	CBA normal	37.9 ± 1.7	
			—	36.4 ± 1.9	
2-b	CBA	A tolerant	A tolerant	16.7 ± 0.9	
			A normal	10.3 ± 0.5‡	38.3
			—	8.9 ± 0.9	
		A normal	A tolerant	15.6 ± 1.1	
			A normal	16.5 ± 0.9	
			—	19.3 ± 1.4	
		CBA tolerant	—	18.8 ± 1.3	
3-a	A	CBA tolerant	CBA tolerant	52.5 ± 3.7	
			CBA normal	40.2 ± 2.9 *	23.4
			A tolerant	35.0 ± 1.7 ‡	33.3
			A normal	39.1 ± 2.3 †	25.5
3-b	CBA	A tolerant	A tolerant	20.8 ± 1.9	
			A normal	14.8 ± 1.3 *	28.8
			CBA tolerant	16.2 ± 0.9 *	22.1
			CBA normal	14.9 ± 1.3 *	28.4
4-a	A	CBA tolerant	CBA tolerant	150.9 ± 5.8	
			CBA normal	120.7 ± 3.8 ‡	20.1
			A normal	126.2 ± 3.2 †	16.4
		CBA normal	CBA tolerant	157.6 ± 7.7	
			CBA normal	149.8 ± 6.9	
			A normal	156.5 ± 9.0	
		A normal	CBA normal	165.3 ± 7.4	
			A normal	153.8 ± 9.1	
4-b	CBA	A tolerant	A tolerant	14.8 ± 1.3	
			A normal	10.6 ± 0.7 †	28.4
			CBA normal	11.9 ± 0.5 *	19.6
		A normal	A tolerant	15.2 ± 0.8	
			A normal	20.3 ± 2.0	
			CBA normal	19.2 ± 1.1	
		CBA normal	A normal	20.1 ± 1.2	
			CBA normal	18.2 ± 1.5	
5-a	CBA	A tolerant	A tolerant	14.4 ± 0.9	
			A normal	9.3 ± 1.1	35.4
			CBA normal	7.8 ± 0.5	45.8
			—	8.5 ± 1.2	
		CBA normal	A tolerant	19.9 ± 1.7	
			A normal	18.9 ± 1.9	
			CBA normal	18.8 ± 1.5	
			—	15.9 ± 1.8	
5-b	A	A tolerant	A normal	48.0 ± 2.5	
			CBA normal	50.6 ± 3.3	
		CBA normal	A normal	46.9 ± 2.1	
			CBA normal	40.6 ± 0.9	

The target cells were exposed to sera from specifically tolerant and normal untreated mice; CBA tolerant = CBA mouse tolerant to A; A tolerant refers to a mouse tolerant to CBA; A normal and CBA normal refer to normal untreated A and CBA mice. Between eight and eleven microwells were included in each group.

Percentage decrease in cell number per microwell with LNC from specifically tolerant donors in the presence of serum from control as compared to the tolerant donors was calculated. Probabilities that the differences between groups receiving control (as compared to "tolerant") serum were due to chance were calculated: * $P=0.05$; † $P=0.01$; ‡ $P=0.001$.

CBA mice tolerant to A grafts, were cytotoxic to cultivated A fibroblasts in the presence of control sera, and that serum from the tolerant animals could nullify that effect. Reciprocal findings were obtained with tolerant A mice. The effect obtained with LNC and sera from the tolerant mice was specific: serum from CBA mice tolerant to A protected cultivated A target cells but did not protect cultivated CBA target cells and vice versa. No abrogation of LNC-mediated immunity was found when serum derived from the strain of target cell origin was added to the cultures. Lymph node cells from tolerant mice had a slight inhibitory effect to syngeneic target cells in experiments 1 and 2-a (as compared with LNC from non-tolerant donors), but did not have any such effect in experiments 2-b and 5.

Although the degree of cytotoxicity detected with LNC from tolerant donors was less than in previous experiments[7-9], the consistency in the data obtained makes it unlikely that they were due to chance. These findings are best explained on the basis of the second hypothesis, according to which the mice were tolerant because they contained serum factors capable of inducing and maintaining the tolerant state. As serum from the mouse strain from which target cells were derived gave no protection, the tolerant state is not likely to be maintained by the circulation of soluble alloantigens capable of binding to otherwise reactive lymphocytes. Such antigens should be present also in mice of the respective target cell strains, unless the additional postulate is made that serum from mice rendered tolerant neonatally contains a special type of tolerogenic antigen. These observations do not make it possible to decide whether the factor abrogating the *in vitro* reactivity of the lymphocytes is an antibody or an antigen–antibody complex, or whether some other type of specific molecule is involved.

It could be argued that the fibroblasts used as target cells *in vitro* have a strain-specific antigen, which is lacking in the spleen cells used to induce "tolerance". In that case, however, the lymphocytes and sera from the "tolerant" mice would be expected to behave like those from normal mice, whereas the experimental results show that the former were presensitized.

Our findings are analogous to those obtained when studying radiation-induced canine chimaeras[7], pregnant mice carrying the conceptus of an allogeneic mating[8], or tumour-bearing individuals whose lymphocytes are immune to specific antigens of the same individuals' neoplastic cells, and who possess blocking serum factors which can specifically abolish the *in vitro* expression of the cell-mediated immunity[9]. Other evidence for the presence of antibodies in "tolerant" mice has been presented by Voison *et al.*[10], who also conclude that this type of tolerance is not the result of induced unresponsiveness.

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Mouse Specific Bone Marrow-derived Lymphocyte Antigen as a Marker for Thymus-independent Lymphocytes

THE usefulness of the theta (θ) alloantigen as a marker for thymus-derived lymphocytes in mice[1-6] has emphasized the need for a distinguishing marker for thymus-independent (bone marrow-derived) lymphocytes, about which relatively little is known. We have raised an antiserum in a rabbit against lymph node cells from mice which had been thymectomized, irradiated and reconstituted with foetal liver cells, which after appropriate absorption was cytotoxic only to those lymphoid cells which were thymus-independent. Because the cell surface antigen(s) with which the antiserum is principally reacting seems to be species-specific, we have followed the example of Shigeno *et al.*[7] and have called it MBLA (mouse-specific bone marrow-derived lymphocyte antigen).

CBA mice were thymectomized when 4–6 weeks old, lethally irradiated (950 r.) and reconstituted with 10^7 syngeneic foetal liver cells after 10–12 weeks. Six weeks later, 185×10^6 lymph node cells from twelve of these mice were injected intravenously into a rabbit, which was boosted intravenously after 1 week with 575×10^6 similar cells and bled out 1 week later. The serum was heat inactivated (56° C for 30 min) and absorbed with 0.1 volume liver, 0.1 volume packed red blood cells (RBC) and six times with 0.1 volume packed thymocytes. Each absorption was carried out at room temperature for 1 h with slow rotation with outbred mouse tissues except for the final two absorptions which were carried out with CBA thymocytes. The serum was tested by chromium-51 and dye exclusion cytotoxic testing using CBA target cells, hamster complement with thymocytes and guinea-pig complement with all other cell types as previously described[8].

Before absorption the rabbit antiserum was of high titre (50% kill at 0.001 against spleen cells) and killed 100% of lymph node, spleen and thymus cells. After the final absorption the serum (now referred to as anti-MBLA) killed approximately 60% of spleen cells and 30% of lymph node cells, but it did not kill thymocytes and its cytotoxic activity for spleen cells could no longer be absorbed with thymus cells.

To establish that the antiserum was not killing thymus-derived lymphocytes, sequential cytotoxic testing was carried out. ^{51}Cr-labelled lymph node cells were first killed with anti-θ (prepared as previously described[1]) and complement, and the residual cells were then tested with anti-MBLA and vice versa. Lymph node cells remaining after lysis with anti-θ were no longer susceptible to anti-θ, but most of the cells could be killed by anti-MBLA (Fig. 1*a*). After lysis with anti-MBLA, the remaining cells were no longer susceptible to the same antiserum but the majority could be killed by anti-θ (Fig. 1*b*). The same result was obtained with ^{51}Cr-labelled spleen cells. This established that the cytotoxic activities of anti-θ and anti-MBLA did not overlap. If all thymus-derived lymphocytes are θ-bearing[1,2,8], then anti-MBLA was not killing thymus-derived lymphocytes. It can be seen in Fig. 1 that a small but significant population of cells in lymph node was not killed by either anti-θ or anti-MBLA, although all the cells were killed by the unabsorbed rabbit antiserum. The nature of these resistant cells is unclear but they could be macrophages or their precursors, granulocytes, a third type of lymphocyte, or a mixture of these, with or without other cell types. As expected, the resistant cell population made up a

Table 1 Results of Dye Exclusion Cytotoxic Testing on CBA Lymphoid Tissues with Anti-MBLA, Anti-θ and Anti-MBLA+Anti-θ

Tissue*	Experiment number	Cytotoxic index† with Anti-MBLA (%)	Anti-θ (%)	Anti-MBLA +anti-θ (%)
Thymus	1	0	>99	—
	2	0	>99	—
Blood	1	33	75	99
	2	34	68	90
Lymph node	1	30	58	86
	2	27	63	86
Spleen	1	58	29	78
	2	55	32	85
Peyer's patches	1	67	40	90
	2	69	31	86
Bone marrow	1	43	0	—
	2	36	0	—

* Cell suspensions were prepared as previously described[6]. More than 90% of the cells were lymphoid, except in bone marrow where 35–45% appeared to be lymphocytes.

† Cytotoxic index=

$$\frac{\%\text{ dead cells with antiserum} - \%\text{ dead cells with normal serum (NMS)}}{100 - \%\text{ dead cells with NMS}}$$

All sera were used neat or diluted 1 : 2, which for both anti-MBLA and anti-θ represented points on a cytotoxic plateau.

In some tests normal rabbit serum (absorbed in same manner as anti-MBLA) was used instead of NMS and gave identical results. In all tests the per cent dead cells with NMS was less than 12%.

larger proportion of the residual lymph node cells after initial lysis with anti-θ than with anti-MBLA (Fig. 1). Because approximately 70% of lymph node cells are θ-bearing[8] compared with 30% MBLA-bearing (Table 1), initial lysis with anti-θ left a relatively small population of residual cells of which cells resistant to anti-θ and anti-MBLA made up a relatively large proportion. The reverse was true when the cells were first killed with anti-MBLA.

The proportion of MBLA-bearing cells in various lymphoid tissues of 3–4 month old CBA mice was studied using dye exclusion cytotoxic testing. As Table 1 shows, the distribution was inversely related to that of θ-bearing cells, and when anti-θ and anti-MBLA were used together they were additive. The fact that anti-MBLA was cytotoxic for spleen cells of 7/7 strains of mice (CBA, A, C57Bl/6, Balb/c, C3H, B10.D2, AKR) and was not cytotoxic for spleen cells of rats, guinea-pigs, hamsters or rabbits, suggests that MBLA is mouse-specific. In absorption studies with homogenates of mouse liver, brain and kidney, only liver absorbed any cytotoxic antibody and this absorption was minimal.

In preliminary experiments, anti-MBLA was found to be cytotoxic for MOPC-315 myeloma cells and when used with complement it inhibited most direct plaque-forming cells (D. W. Dresser and M. Raff—unpublished observations). It is therefore clear that MBLA is present on the surface of resting marrow-derived lymphocytes (antibody-forming cell precursors =AFCP) as well as on actively secreting antibody-forming cells (AFC), which we think develop from marrow-derived lymphocytes[9]. This is in contrast to the PC_1 alloantigen in mice which seems to be present only on AFC (ref. 10). A preliminary experiment showed that anti-MBLA inhibited 82%, anti-θ 22% and both together 97% of immune spleen rosette-forming cells against sheep RBC (M. F. Greaves and M. C. Raff, unpublished observations). It is unlikely that the cytotoxic or inhibitory activity of anti-MBLA is caused by anti-immunoglobulin antibodies, for the serum did not react in Ouchterlony testing with normal mouse serum (NMS) and its cytotoxic activity was unaffected by the presence of NMS. At the moment, the possibility that the antiserum kills a proportion of non-lymphoid cells (such as granulocytes and/or macrophages) as well as thymus-independent lymphocytes cannot be excluded.

The use of heteroantibodies to distinguish different types of lymphocytes reported here and by others[11–13] suggests that this approach may be fruitful in man. Besides its theoretical and diagnostic value, an anti-lymphocyte serum which was specific for human antibody-forming cells and their precursors could well have therapeutic application in view of the possible role of enhancing antibodies in tumours[14].

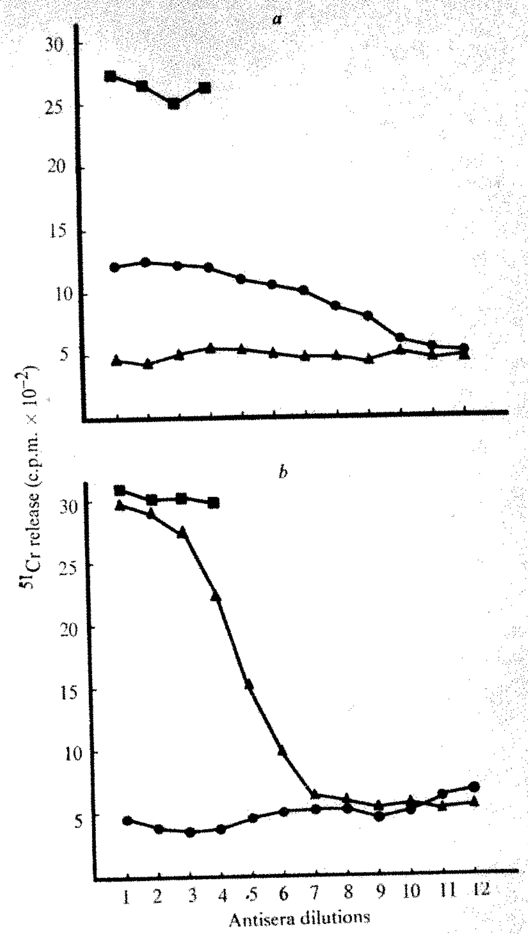

Fig. 1 Sequential ^{51}Cr cytotoxic tests. CBA lymph node cells were labelled with ^{51}Cr and killed with anti-θ and complement (*a*) or anti-MBLA and complement (*b*). [50×10^6 cells were incubated with 1 ml. of antiserum diluted 1 : 2 for 30 min at 37° C, washed and similarly incubated with 1 ml. of guinea pig complement diluted 1 : 3.] After washing, the residual cells were tested with anti-θ (▲), anti-MBLA (●) and the unabsorbed rabbit antiserum (■), with neat serum in the first tube in each case.

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Quinacrine Fluorescence of the Human *Y* Chromosome

RECENT observations[1-4] of specific localized fluorescence in *Y* chromosomes stained with quinacrine mustard and quinacrine hydrochloride have provided a new parameter for the study of abnormal *Y* chromosomes. We have re-examined regularly prepared chromosome and buccal smear slides of at least 100 cells from two patients with a small *Y* chromosome[5] and from patients with normal *Y* chromosomes. We used a modification of techniques described earlier[1-4]. We stained for 5 min in 0.5% quinacrine hydrochloride (Winthrop); washed in distilled water; differentiated for 3 min in citric acid–phosphate buffer, *p*H 5.5; washed and mounted slides in phosphate buffer, *p*H 7.4, and sealed with nail polish. Preparations were examined with a Leitz Ortholux microscope with a mercury arc lamp, standard fluorescence filters, and dark-field illumination, and were photographed with Ektachrome high speed film. Fluorescence persisted for several days. Full details of the technique will be published later.

Fig. 1 Interphase nucleus showing two adjacent fluorescent bodies.

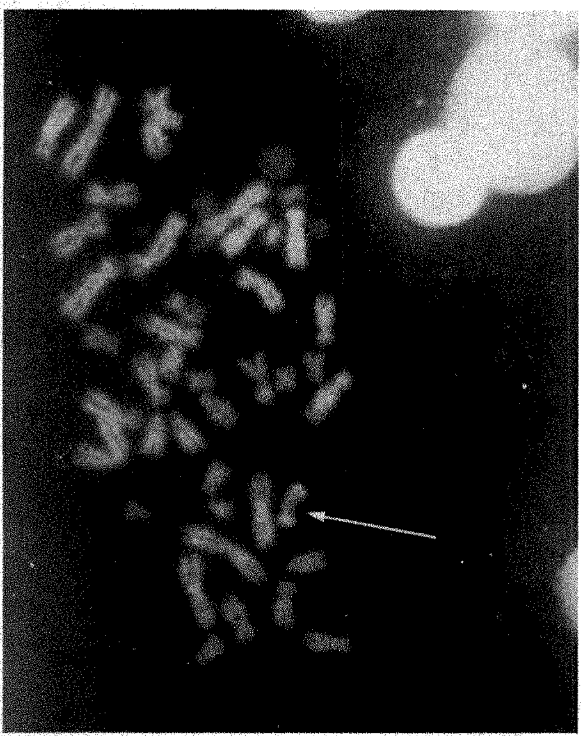

Fig. 2 Metaphase spread showing two fluorescent regions on the dicentric *Y* chromosome.

The distal portion of the long arm of the normal *Y* chromosome fluoresced clearly and distinctly in metaphase plates and a corresponding fluorescent particle was present in many interphase nuclei, but no comparable fluorescence was detected in preparations from patients with a small *Y* chromosome. This may be because of deletion of the heterochromatic region in the long arm.

We have also investigated a patient with a dicentric chromosome, and found two adjacent fluorescent spots in interphase nuclei (Fig. 1), and could see two fluorescent spots on both the distal ends of the dicentric *Y* chromosome (Fig. 2). It will be interesting to study patients with an iso-chromosome of the long arm of *Y* with this technique. One could expect to see two fluorescent regions in these patients.

We have previously shown that fertility and other sexual characteristics are normal in men with a small *Y* chromosome[5]. The observation described here indicates that maleness is not dependent on the presence of a fluorescent region in the long arm of the *Y* chromosome. Caution may therefore have to be exercised in using the quinacrine fluorescence technique for determination of the *Y* chromosome[6].

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Use of the *Y* Chromosome in Prenatal Sex Determination

REPEATED observations of the cellular composition of human endocervical mucus from the earliest weeks of pregnancy, using various staining techniques, have revealed not only cells of maternal origin, but also chorionic cells which have been shed into the fairly static cervical mucous plug.

I have used the fluorescein dye test[1-4] on smears taken with a cotton swab from the mid-cervical mucus of thirty patients in the first, second and third trimesters of pregnancy. In eighteen cases quinacrine hydrochloride revealed in a proportion of the interphase chorionic nuclei a single fluorescent spot, indicative of *Y* chromosome material, and thus of a male conceptus. In the other twelve patients smears developed no fluorescent spot, indicative of a female conceptus. Six of the eighteen have now been delivered of boys and four of the twelve have produced girls. These observations are being extended.

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Identification of *Y* and *X* Chromosomes in Amniotic Fluid Cells

A FLUORESCENT staining technique has been described[1–3] for identification of the *Y* chromosome in cells from various sources. The use of this technique to detect *Y* chromosomes in the amniotic fluid cells, in conjunction with a search for sex chromatin bodies in these cells, might provide a rapid and accurate means of prenatal sex determination.

Fresh amniotic fluid from twelve women whose pregnancies were being terminated was centrifuged at 800–1,000 r.p.m. for 20 min, the supernatant discarded and a smear of the cell pellet was prepared. Smears were fixed in methanol for at least 15 min, stained with a 0.5% aqueous solution of quinaquine dihydrochloride for 5 min, washed in running tap water for 3 min and rinsed in 0.2 M acetate buffer (sodium acetate; glacial acetic acid), *p*H 5.5. The preparations were mounted in 1 : 1 glycerol and buffer. A minimum of 100 cells was examined from each specimen. In four specimens a fluorescent body (*Y* chromosome) was detected in 3–9% of the cells.

Sex chromatin was determined in eight specimens. One drop of the cell pellet of the amniotic fluid was mixed and stained immediately with one drop of 2% aceto-orcein and then compressed with a cover slip. Immediately after preparation the slides were examined for sex chromatin bodies. Two were sex chromatin positive, two were negative, four were unsatisfactory because there were too many pyknotic cells and too few cells suitable for analysis according to the selection criteria suggested by Hsu *et al.*[4]. All studies were done before expulsion of the foetuses. The results of *Y* fluorescence, sex chromatin and phenotypic sex determination for each abortus are shown in Table 1.

Pathological examination of the abortuses revealed five males and seven females. Although the four smears which developed fluorescent bodies were from males, one other male could not be detected by the method used. The reasons for our failure to detect a fluorescent body in the amniotic fluid cells are now being investigated. One possibility is that many of the cells were damaged or not viable, and this certainly seemed to account for the unsatisfactory smears for sex chromatin determination. The other possibility is that a small *Y* chromosome may fail to fluoresce. Borgaonkar and Hollander[5] found a male with a small *Y* chromosome which did not fluoresce. We have recently had two cases where no sex chromatin body was found in 200 amniotic fluid cells and karyotypes of the fibroblasts cultured from one amniotic fluid revealed a 46,*XX* chromosomal constitution. No karyotypes were done on the other fluid, but both foetuses were found to be phenotypic females (our unpublished results).

Based on these observations, we feel that extreme caution should be used in prenatal sex determination by examination for fluorescent *Y* and sex chromatin body. While the finding of a fluorescent body does indicate the presence of a *Y* chromosome and the presence of a sex chromatin body indicates the presence of an inactivated *X* chromosome, the failure to detect these bodies does not necessarily indicate the absence of the corresponding chromosome. It seems that until further experience with these techniques is obtained, karyotype analysis of cultured fibroblasts from amniotic fluid cells is the only accurate means of prenatal sex chromosome determination.

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Table 1 *Y* Chromosomes, Sex Chromatin and Phenotypic Sex of Twelve Abortuses

Case No.	1	2	3	4	5	6	7	8	9	10	11	12
Y fluorescence	+	–	–	–	–	+	+	–	–	–	–	+
Sex chromatin	ND	ND	ND	ND	NS	NS	–	NS	+	NS	+	–
Phenotypic sex	M	F	F	F	M	M	M	F	F	F	F	M

ND, Not done; NS, not satisfactory; M, male; F, female; +, positive; –, negative.

Persistent Alteration of Turnover of Brain Noradrenaline in the Offspring of Rats subjected to Stress during Pregnancy

VARIOUS hypotheses have suggested that environmental stress during development is an aetiological factor in mental illnesses. Such hypotheses have included both biological and psychoanalytical concepts, but they have not explained convincingly any possible mechanism of action of stress. The developing organism has often been shown to be sensitive to various hormonal influences, and steroid and thyroid hormones or stress, given at a critical time during the neonatal period, seem to affect permanently the behaviour and metabolism of growing animals[1–3].

There have been several reports that stress or injections of adrenaline given to pregnant rats can have a persistent, although variable, effect on the behaviour of their progeny[4–10]. Although these changes in the offspring are probably mediated by some biological mechanism, they cannot be explained by any known persistent neurobiological changes. We have therefore made a neurochemical examination of the progeny of stressed pregnant rats, which could be a preliminary step in the construction of an animal model for human mental illnesses. We found that when stress was applied during pregnancy there was a long lasting effect on the metabolism of cerebral noradrenaline in the offspring.

Pregnant Sprague–Dawley rats were stressed from the fifteenth to nineteenth day of pregnancy with daily foot-shocks (BRS Foringer shock generator scrambler No. 001, 0.040 W for 5 min each day). When, in preliminary experiments, the shocking was continued beyond the nineteenth day of pregnancy, stressed mothers often ate their young. During the daily 5 min period of stress two pregnant rats were kept in the same cage. They frequently displayed either overt fighting behaviour or assumed a stereotyped fighting posture, rearing on their hind legs during the session. Control mothers were kept in similar cages equipped with a metal grid base for an equal time without the shocks. On the twentieth day of pregnancy, control and experimental rats were placed in individual cages until the birth of their offspring. Litters of eight to twelve rats each, of control and experimental mothers, were born on the same day after an average pregnancy of 21–22 days. After delivery the cages were not opened nor were the newborn rats handled before the age of 10 days. They were separated from their mothers at the age of 21–23 days.

Table 1 Effect of Prenatal Stress on the Turnover of Noradrenaline in the Rat Brain

		Concentration of noradrenaline (ng/g)	Specific activity (d.p.m./ng of ^{3}H-noradrenaline) 1 h	3 h
First experiment				
Telencephalon–diencephalon–anterior mesencephalon	Control	492 ± 29 (14) (100%)	1,344 ± 50 (7) (100%)	893 ± 63 (7) (100%)
	Experimental	480 ± 27 (14) (97%)	1,261 ± 76 (7) (94%)	689 ± 64 (7) (77%)*
Second experiment				
Telencephalon–diencephalon	Control	257 ± 28 (7) (100%)	—	836 ± 70 (7) (100%)
	Experimental	289 ± 11 (7) (112%)	—	566 ± 52 (8) (68%)†
Brain stem–mesencephalon	Control	510 ± 40 (6) (100%)	—	1,243 ± 120 (7) (100%)
	Experimental	627 ± 23 (7) (123%)*	—	1,001 ± 74 (8) (80%)

Data are mean + s.e.m. (N) (% control). * $P < 0.05$. † $P < 0.01$.

The offspring of the stressed rats grew at the normal rate, and they had no gross neurological or behavioural abnormalities. At the age of 40–45 days the turnover of brain noradrenaline of the males was estimated by measuring the rate of disappearance of intracisternally injected radioactive noradrenaline. Under light ether anaesthesia, 5 µCi of 7-L-^{3}H-noradrenaline (2.2 µCi/mmol, Amersham/Searle) was injected in 25 µl. of physiological medium[11]. After 1 or 3 h rats were decapitated, and brains and spinal cords were removed and dissected; the cerebellum was discarded. In each experiment, the control and experimental animals were from litters born on the same day, and the control and experimental animals were killed alternately. In the first of two experiments, the brain was divided by transection at the rostral limit of the pons, and the anterior part (telencephalon–diencephalon–upper mesencephalon) was studied. In the second experiment a transection was made just above the corpora quadrigemina and at the caudal limit of the medulla, and two regions were produced: the first region included the telencephalon and diencephalon, and the second region included the mesencephalon and brain stem. The separate brain regions were weighed while wet, and extracted in 12.0 ml. of 0.4 N perchloric acid in a motor-driven glass Potter–Elvehjem homogenizer and the homogenates were centrifuged at 10,000*g* for 20 min. Noradrenaline was isolated from the supernatants by adsorption on alumina chromatography columns[12]. Endogenous noradrenaline in an acid eluate of the alumina columns was measured by a fluorometric method[13], and the radioactivity of the fraction was measured by liquid scintillation spectrometry[14]. Corrections were made for the recovery of ^{3}H-noradrenaline and endogenous noradrenaline from the columns.

The rate of decrease of the specific radioactivity of noradrenaline in telencephalon–diencephalon was found to be greater in the male offspring of the stressed rats, suggesting a faster turnover of brain noradrenaline in these animals. The half life of radioactive noradrenaline as estimated from the 1 and 3 h points was approximately 3.4 h in the control group but only 2.5 h in the experimental group (Table 1). In the second experiment, the increased rate of disappearance of radioactive noradrenaline in telencephalon–diencephalon was confirmed (Table 1). A smaller change, which failed to attain statistical significance, was also found in the mesencephalon–brain stem. Because the amounts of ^{3}H-noradrenaline found in brains of both groups of rats were not different 1 h after intracisternal injection, it is unlikely that prenatal stress led to a decrease in the uptake of labelled amine. The concentrations of endogenous telencephalic–diencephalic noradrenaline were not significantly changed in either experiment, but in the second experiment the concentration was significantly increased in the brain stem (23%) (Table 1). Although this change in the concentration of noradrenaline in the brain stem needs further confirmation, it lends support to the conclusion that the turnover of this compound in the brain was increased after prenatal stress.

This increased turnover in the brains of 40–45 day old male rats after stress to their mothers during pregnancy could be a consequence of prenatal or postnatal effects[10]. For example, the rearing habits of the stressed mothers may have been altered. By using a cross-fostering technique, or allowing normal foster mothers to raise the offspring of both the control and stressed mothers it might be possible to resolve this question. But in our previous experiments both stressful neonatal handling (5 min each day) and intraperitoneal injections of adrenaline (10–20 µg in oil, Parke Davis) of the newborn rats from the second to the tenth postnatal day had no effect on the turnover of noradrenaline. It seems more probable, therefore, that the effects we have noted were brought about during the development of the foetus. The effects of maternal stress could be mediated through a release of adrenal medullary catecholamine or corticosteroid hormones, both of which can cross the placenta and possibly enter the central nervous system *in utero*[15]. The effects of injections of adrenaline and hydrocortisone during the same gestational period on the turnover of noradrenaline in the progeny are now being investigated.

The increased turnover in the brain does not necessarily reflect changes in the resting metabolic rate of this putative neurotransmitter. The noradrenaline in the brain is quite sensitive to various stresses[16], and the offspring of stressed mothers could be merely more responsive to the stress of the intracisternal injection procedure. In this case, the change in metabolism of noradrenaline produced by prenatal stress would not be an isolated specific alteration of metabolism. Extensive (neuro)chemical and (neuro)histochemical screening will therefore be necessary to determine the entire metabolic sequences of prenatal stress.

The relevance of animal experiments to human studies can always be challenged. This is especially true in this case, for the time course of the development of rat brain is markedly different from that of man[17]. Rats are born relatively immature, and the greatest increase in the weight of developing rat brain occurs under considerable environmental stress after the birth, while in man this critical period of development occurs in the more stable and isolated conditions of the uterus. Therefore, the effects of stress even during the corresponding period of ontogeny may be quite different in man and in rat. Some other animals, for example the guinea-pig, could perhaps better serve as a model for human studies.

In spite of the difficulties of comparing different species, it is possible that intra-uterine experiences in man may also induce changes in brain metabolism, some of which might be sustained after birth and might alter behaviour[15,18]. It is, however, too early to speculate about the theoretical implications of our observations for the aetiology of human mental illnesses. Nevertheless, it is interesting that in some recent epidemiological studies an abnormally high incidence of complications during pregnancy and delivery has been found among the schizophrenics[19,20].

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Reduction or Disappearance of Visual After Effect of Movement in the Absence of Patterned Surround

THE apparent movement of stationary patterns in the opposite direction to their immediately preceding real movement is among the earliest reported and most extensively investigated visual after effects[1-3]. We have shown that the visual movement after effect is reduced or eliminated in the absence of a patterned surround, and that the presence of a surround is a stimulus condition necessary for its occurrence. Surround variables must, in future, be taken into account in explaining the movement after effect phenomenon.

The moving or stationary target was a pattern of vertical light and dark bars behind a 6 cm diameter circular aperture subtending a visual angle of 3° at the observation distance of 152 cm. The bars were 1.9 cm wide (0.75°) and were illuminated from behind. During the stimulation period of 90 s the bars moved from left to right at 2.25° s^{-1} and during the test period, which followed immediately, the bars were stationary. Depending on ambient light the luminance of the light bars was between 7.30 and 11.92 cd m^{-2}, insufficient alone to cause variations in the movement after effect[4]. Without room lights, only the light bars of the moving target were visible. A central fixation point was marked on a clear plastic cover over the aperture. After 90 s of fixation during movement of the bars, the observer recorded apparent opposite motion of the stationary bars by manually moving a carriage to track apparent movement and to record it on a moving chart. Tracking the movement after effect by hand motion, also used by Honig[5], was preferred to the more common methods of estimating its duration and "cancelling" it by a counter-movement of the target. The validity of this method has been established by requiring observers to track slow real movement.

The first experiment followed the chance observation that after fixation of the target in darkness there was little or no movement after effect. Four conditions were arranged to investigate this reduction and to establish whether it is due to the surround being dark and without pattern during either or both (stimulation and test) phases. A circular, 66 cm diameter surround (24°) with vertical, 1.9 cm (0.75°) wide black and white bars was mounted concentrically around the target and illuminated indirectly by incandescent sources so that the luminance of the light bars was 11.92 cd m^{-2}. The target of nearly constant luminance was clearly visible throughout. Referring in order to the stimulation and test phases and to the patterned and dark surrounds as P and D respectively, the four conditions were PP, PD, DP and DD. Twenty-four people observed in all conditions, each in one of the twenty-four possible orders. After three familiarization trials, observers were given a 10 min break and then the four test trials with 3 min breaks between. Mean movement after effects are shown as cumulative apparent distance moved by the bars over 10 s in Fig. 1*A*. The movement after effect for DD was markedly less than that for PP with those for DP and PD intermediate. One of the twenty-four observers failed to indicate a movement after effect in PP, two in DP, seven in PD and eleven in DD.

Differences in movement after effect due to absence of surround in inducing and test phases were both significant (inducing phase, *F*, 1,23 = 17.54, *P* 0.001; test phase, *F*, 1,23 = 37.81, *P* 0.001). Moreover, the movement after effect for PD was half that of DP, suggesting that the surround pattern is more significant in the test than in the inducing phase.

It is unclear from these findings whether the diminished movement after effect is due to sheer absence of light or lack of visible pattern in the target surround. In a second experiment twenty-four observers recorded the movement after effect as the luminance of the patterned surround was reduced from 11.17 to 0.11 cd m^{-2}. This large reduction in surround luminance reduced the movement after effect only marginally. This suggested that absence of pattern in the surround rather than

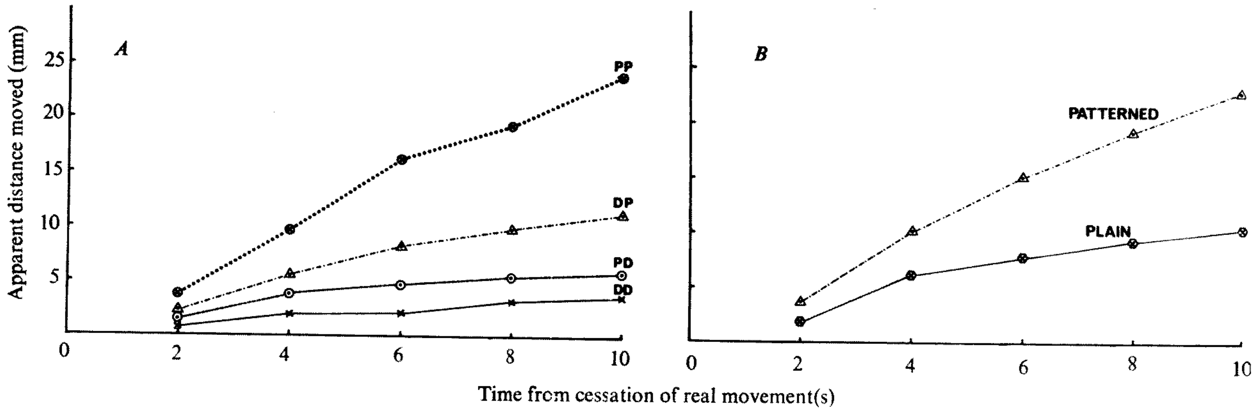

Fig. 1 (*A*) Cumulative apparent distance moved by stationary bars during 10 s in experiment 1. P, Patterned surround and, D, dark surround during stimulation and test phases in that order. (*B*) Cumulative apparent distance moved by stationary bars during 10 s in experiment 3 with patterned and plain surround.

absence of light was the critical determinant. A third experiment was therefore conducted, using the patterned surround of the two earlier experiments and a plain white surround of the same size, shape and material. The luminance of the light area of both surrounds was 0.11 cd m^{-2}. Twelve subjects observed with both surrounds with the orders and presentation counterbalanced (Fig. 1*B*). With the plain surround the movement after effect was much less than with the patterned surround (*F*, 1,11 = 7.30, *P* 0.05). Since the total light reflected from the plain white surround was greater than from the barred pattern it can be concluded that the reduced movement after effect with a uniform dark or light surround was a consequence chiefly of the absence of visible pattern.

In another experiment with twelve subjects, we found that there was no significant difference in the movement after effect produced when the surround pattern consisted of regularly arranged dots, concentric circles, a grid pattern or vertical bars. Thus while a patterned surround is a critical determinant of the movement after effect, the particular pattern is not. Variables such as orientation of surround contours, however, require systematic investigation.

In experiments with rotated sectored disks we have obtained a less striking reduction in the movement after effect than that occurring with linear moving targets in the absence of surround pattern.

Visual movement can be classified conveniently as relative or egocentric movement. In the case of relative movement objects are observed to move relative to other stationary or moving objects, but with egocentric movement they are observed as moving relative to the observer only, for the visual field is dark or featureless. The findings reported here indicate that the movement after effect is essentially a relative movement phenomenon, and it can be assumed that the neural processes correlated with the after effect derive from stimulation by moving and stationary contours. This finding is supported by Wohlgemuth's observation[3] that the after effect occurs only feebly after movement of the total visual field. If, as suggested[6,7], the neural processes associated with the movement after effect are indicative of those involved in real movement, it is reasonable to suppose that the latter is encoded in relative terms.

It has occurred to us that the presence of a patterned surround may also be a significant determinant of other after effects such as those associated with tilted contours[8] and orientation specific after images obtained with stationary and moving patterns[9-11].

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Primary Reaction of Phytochrome

MANY aspects of morphogenesis in higher plants are regulated by phytochrome[1,2], but the mechanism of its action is still a subject for controversy[3]. By "primary reaction of phytochrome" we mean the first reaction in which P_{FR}, the physiologically active species of the phytochrome system which absorbs far red light, becomes involved after its formation ($P_{FR}+X \rightarrow P_{FR}X$). This reaction has not yet been identified. The chief problem is whether or not the reaction partner or reaction site X is the same in all photoresponses mediated by phytochrome. For some reason it is generally believed that the primary reaction of P_{FR} is the same in all cells[3]. With the same confidence, however, one can maintain that, even in the primary reaction, P_{FR} acts differently in different cells or in different compartments of a particular cell[2].

Recent findings support the latter alternative. There are at least two sets of data which relate to this problem. First, while the results obtained by Hartmann[4,5] with lettuce seedlings (hypocotyl lengthening) and by Oelze-Karow *et al.*[6] with mustard seedlings (threshold regulation of lipoxygenase synthesis) probably require a cooperative model for the primary reaction of P_{FR}, Lange *et al.*[7] have shown for phytochrome-mediated anthocyanin synthesis in the mustard seedling that there is no need to postulate any cooperative effect between P_{FR} molecules. Second, while for phytochrome-mediated photomodulation of ascorbic acid synthesis in the mustard seedling, the control by P_{FR} is independent of RNA synthesis[8], phytochrome-mediated anthocyanin synthesis[7,9] and a number of other responses[2] probably involve regulation of gene activity.

Here we compare some details of phytochrome-mediated ascorbic acid and anthocyanin synthesis in the same system (mustard seedling, *Sinapis alba* L.). Our data are relevant to

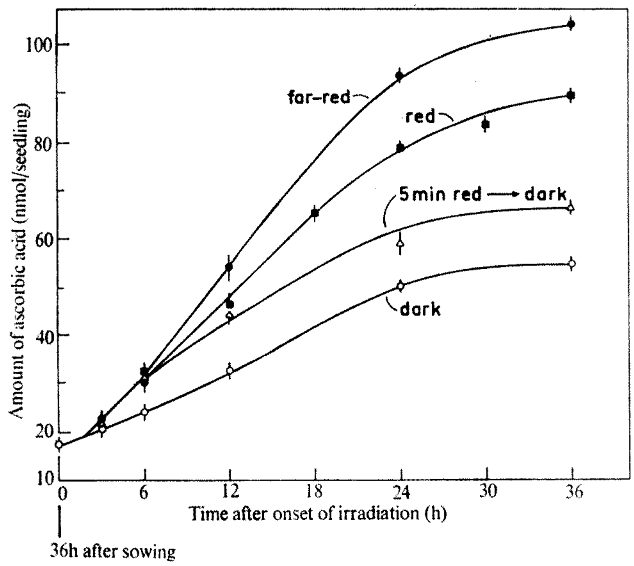

Fig. 1 Time course of ascorbic acid accumulation under continuous far red light, continuous red light and after one brief irradiation (5 min) with red light given at time zero (that is, 36 h after sowing).

the problem of whether or not the primary reaction of P_{FR} is the same in both responses.

Seed of white seeded mustard was bought from a commercial grower (Schoell, Stuttgart). Selection of seeds and treatment of seedlings followed the standard techniques for photomorphogenic research with mustard seedlings developed in our laboratory[10]. The seedlings were grown at 25.0±0.2° C in the dark, and light treatment was started 36 h after sowing—time zero in the figures.

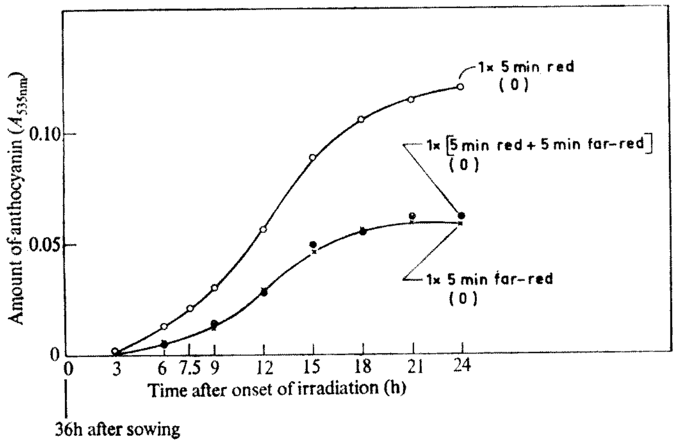

Fig. 2 Time courses of anthocyanin accumulation after one or two brief irradiations (5 min each) with red light, far red light, or red followed by far red light. The irradiations were performed at time zero (that is, 36 h after sowing).

For irradiation, the standard red[11] and far red[10] sources were used at an irradiance of 67.5 μW cm^{-2} ± 10% (red) and 350 μW cm^{-2} ± 10% (far red). The temperature during irradiation was 25.0±0.4° C. The methods of extraction and determination of ascorbic acid and anthocyanin have been described elsewhere[8,9,12]. The values in the figures are means of between eight and sixteen parallel but independent experiments. Standard errors were about 2–5% (or indicated by the vertical bars).

Five minutes of red light (which establishes a phytochrome photoequilibrium of about $[P_{FR}]/[P_{TOT}] = 0.8$) applied to a dark grown seedling at time zero will transiently increase the rate of ascorbic acid accumulation (Fig. 1). Because the effect of 5 min of red light can be fully reversed by an immediate irradiation with 5 min of far red light[12], we conclude that P_{FR} in the ground state (non-excited) can effectively control the rate of ascorbic acid accumulation. Similarly, 5 min of red light applied to a dark grown seedling at time zero causes anthocyanin synthesis (Fig. 2), and as the effect of 5 min of red light can be fully reversed by immediately following it with 5 min of far red light (Fig. 2), we conclude that P_{FR} in the ground state can cause anthocyanin synthesis.

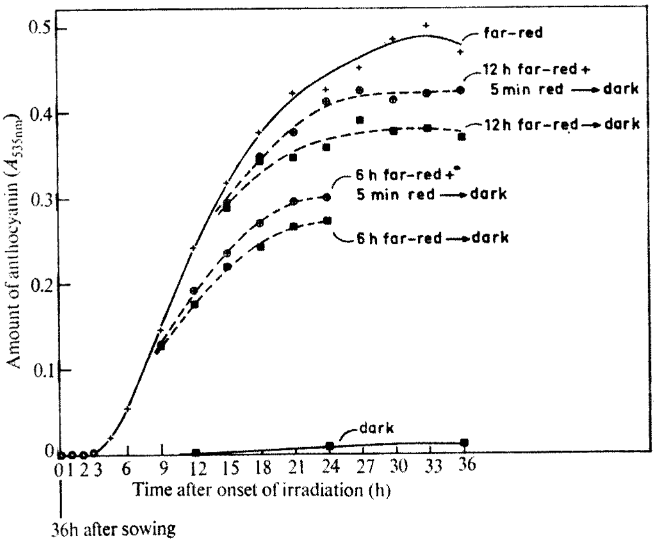

Fig. 3 Time courses of anthocyanin accumulation under continuous far red light and in experiments where the standard far red light was turned off 6 or 12 h after the onset of irradiation. The samples were either placed in the dark immediately or received 5 min red light before the transfer to darkness.

Continuous far red light (which will establish a phytochrome photoequilibrium of about $[P_{FR}]/[P_{TOT}] = 0.03$) exerts a strong effect on anthocyanin synthesis (Fig. 3). The rate of anthocyanin synthesis in the linear part of the curve is a log function of the irradiance in these circumstances[7]. This dependency on irradiance in conditions of continuous irradiation is a characteristic of the so-called "high intensity reactions". According to

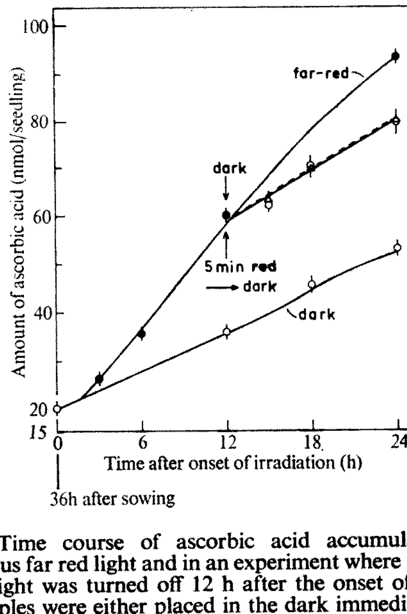

Fig. 4 Time course of ascorbic acid accumulation under continuous far red light and in an experiment where the standard far red light was turned off 12 h after the onset of irradiation. The samples were either placed in the dark immediately or they received red light for 5 min before the transfer to darkness.

Hartmann[4,5], this effect can be attributed to the phytochrome system as well. And indeed, we have found no data which could not be reconciled with the hypothesis advanced and supported by Hartmann[13] that the morphogenic effects of continuous light of wavelength greater than 550 nm can be attributed to phytochrome[7]. Fig. 3 shows that even after prolonged treatments with continuous far red light, the anthocyanin producing system of the mustard seedling responds to changes of the P_{FR} level (exerted by 5 min of red light after the termination of far red light) as would be expected: an increase of P_{FR} in the ground state from about 3% P_{FR} (photoequilibrium characteristic for red light) leads to an increase in the rate of anthocyanin synthesis. Corresponding experiments for ascorbic acid accumulation lead to a different result (Fig. 4). The ascorbic acid synthesizing system of the mustard seedling does not respond at all to changes in the level of P_{FR} (exerted by 5 min of red light after the termination of far red light). The programme: 12 h far red light plus 5 min red light→dark leads to the same results as the programme: 12 h far red light→dark. Obviously the system can no longer respond to P_{FR} in the ground state while the sensitivity towards continuous far red (that is, phytochrome in some excited state) is not significantly decreased.

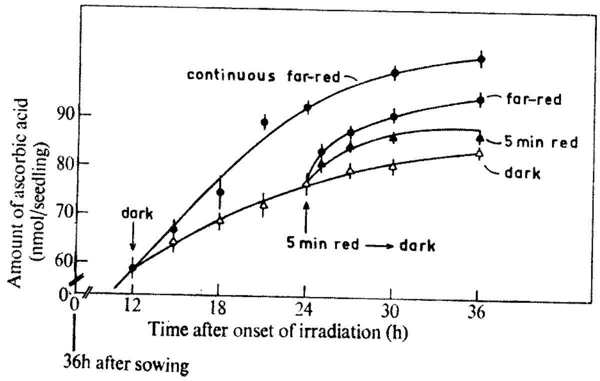

Fig. 5 Time course of ascorbic acid accumulation under the programme: 36 h dark (time zero)—12 h far red light—12 h dark—5 min red light→dark. The corresponding control kinetics are given as well: 12 h far red light→dark (dark); 12 h far red light—12 h dark→far red light (far red); continuous far red light.

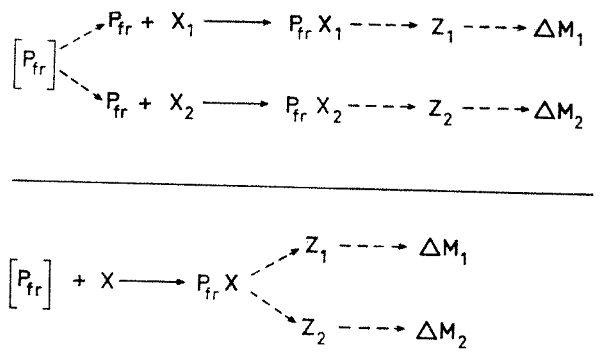

Fig. 6 Two alternative models of the primary reaction partner (or site) of P_{FR} (in the ground state). The lower model is not consistent with the facts reported in this paper. While other, more complicated, models might be conceived to explain the available experimental information, the upper model has the advantage of being simple as well as consistent with the facts. $[P_{FR}]$: P_{FR}-pool of the system; $X_{1,2}$: reaction partner(s) or site(s) of P_{FR}. Nothing is implied about the degree or type of difference between the different Xs. $Z_{1,2}$, intermediate(s) between $P_{FR}X$ and the responses; ΔM: extent of P_{FR} mediated responses (in the present case, increase of rate of synthesis).

The question arises as to whether or not the sensitivity of the system towards P_{FR} in the ground state can be restored by a dark period. This is indeed the case. Fig. 5 shows that after a dark period of 12 h (following 12 h of continuous far red light) the ascorbic acid synthesizing system of the mustard seedling again responds to P_{FR} even in the ground state (5 min red→dark).

The anthocyanin synthesizing system and the ascorbic acid accumulating system of the mustard seedling clearly respond differently to a treatment with continuous far red light. For anthocyanin synthesis, sensitivity towards P_{FR} (in the ground state) is preserved, but for ascorbic acid accumulation it is lost after 12 h of continuous far red light. In both cases, however, sensitivity towards continuous far red (P_{FR} in some excited state) did not change significantly during the experimental period (compare Figs. 3 and 4, continuous far red). Under continuous far red light both responses (anthocyanin synthesis as well as ascorbic acid accumulation) follow virtually steady state kinetics during the experimental period (between 6 and 18 h after the onset of irradiation). Any model which claims to describe the universal reaction, $P_{FR}+X \rightarrow P_{FR}X$ (ref. 3), must explain these facts. We feel that such a universal model is difficult to formulate if it is at all feasible. For this reason we prefer the hypothesis (Fig. 6) that X is not the same for every plant photoresponse. We frankly admit that a detailed model of the process $P_{FR}+X_i \rightarrow P_{FR}X_i$ is not available at the moment, neither for phytochrome-mediated ascorbic acid accumulation nor for phytochrome-mediated anthocyanin synthesis. We hope, however, that results like those presented here will open the way to a better understanding of the primary reactions of P_{FR}, for we have good reason to ask: "What is the primary reaction of P_{FR}?" for every sort of photoresponse.

We propose the hypothesis that the reaction partner (or site) of P_{FR} (X) can be different in different cells or in different compartments of a particular cell and that for this reason we can expect a multiplicity of "primary reactions of P_{FR}".

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Coupled Oscillatory Control Mechanism in a Planktonic System

THE mechanism by which soluble organic matter is released in lakes and the rate at which this occurs are of great importance relative to the development and rate of metabolism of populations of heterotrophic bacteria. One potentially large source of soluble organic matter is extracellular release by phytoplankton which are actively photosynthesizing. It has been shown that rates of excretion of organic matter by algae are a function of the relative growth rate of the algae in culture[1,2]. In conditions of constant light, there is a tendency for the net excretion rate to be more or less constant initially and then to approach zero after 3–5 h.

Glycollic acid, amino-acids, sugar alcohols, peptides and polysaccharides have been the principal substances detected in excretions of algal cultures[3,4]. The simple substrates excreted are probably derived from small metabolic pools that are saturated very soon after exposure to light[5]. There is evidence that *Thallassiosira fluviatilis* excretes largely newly formed organic matter, although a small percentage of the carbon excreted may come from older cellular constituents[4].

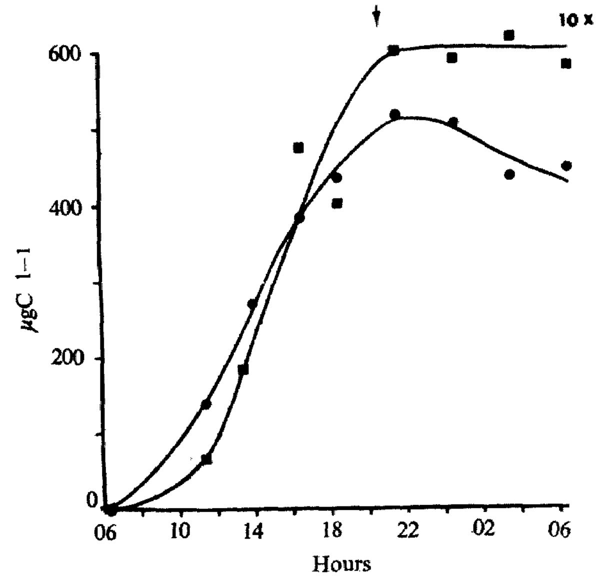

Fig. 1 Net photosynthetic carbon fixation and extracellular release by phytoplankton at 1 m in Frains Lake, Michigan, July 22, 1968. ●—●, Photosynthesis; ■—■, extracellular release. Arrow indicates sunset.

The kinetics of extracellular release, throughout a 24 h period, of soluble organic matter by phytoplankton *in situ* have not previously been examined in detail, although *in situ* experiments have been conducted during the mid-solar day[3]. Fig. 1 shows an example of cumulative net photosynthetic carbon fixation and extracellular release by phytoplankton at 1 m in Frains Lake, Michigan, on July 22, 1968. NaHC^{14}O$_3$ was used as a tracer. It is assumed that the extracellular organic matter is derived entirely from newly formed photosynthate. The amount released can thus be calculated directly knowing the specific activity of the inorganic pool available for photosynthesis. During the daylight period the rates of both processes fluctuate from zero to some high value and back to zero. The rates would fluctuate even if the extracellular matter was derived from older cellular material. The average hourly rates of net photosynthetic fixation and extracellular release are plotted in Fig. 2. In this case the excretion rate lags behind the photosynthetic rate, with the maxima differing by approximately 4 h.

If the enzyme systems for the bacterial community are not saturated initially for the substrate released extracellularly, the metabolic rate of the bacteria could be predicted to vary with the concentration of substrate. This rate would vary approximately as the assimilation rate of substrate according to the well known Michaelis-Menten enzyme kinetics. Some adjustment of the bacterial enzyme systems to increasing levels of substrate might also be expected, particularly at high levels. Thus the response of the bacteria would lag behind the release of substrate by the phytoplankton. The rate of assimilation would decrease again as the substrate was assimilated by the bacteria.

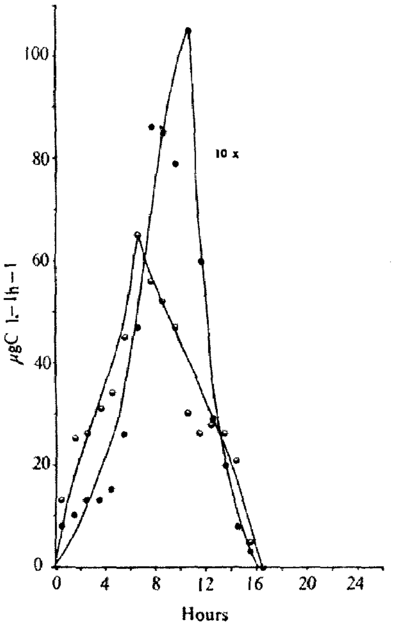

Fig. 2 The average hourly rate of net photosynthetic fixation and extracellular release by phytoplankton at 1 m in Frains Lake, Michigan, July 22, 1968. ◒—◒, Photosynthesis; ●—●, extracellular release.

We carried out a simulation experiment to test for a fluctuation in the rate of assimilation by the bacteria of an extracellular soluble organic pool. Unmodified water from the lake surface was placed in a 5 gallon carboy which was then suspended at the surface of the lake. Glucose was added to the carboy hourly at a rate which simulated a known rate of extracellular carbon release by natural phytoplankton communities (Fig. 3) in a productive lake. The experiment was initiated at sunrise and was terminated the following sunrise. At hourly and later two hourly intervals the carboy was subsampled. Duplicate 300 ml. biochemical oxygen demand (BOD) bottles were filled with the subsample and inoculated with tracer quantities of glucose-C-14(U). The bottles were wrapped with

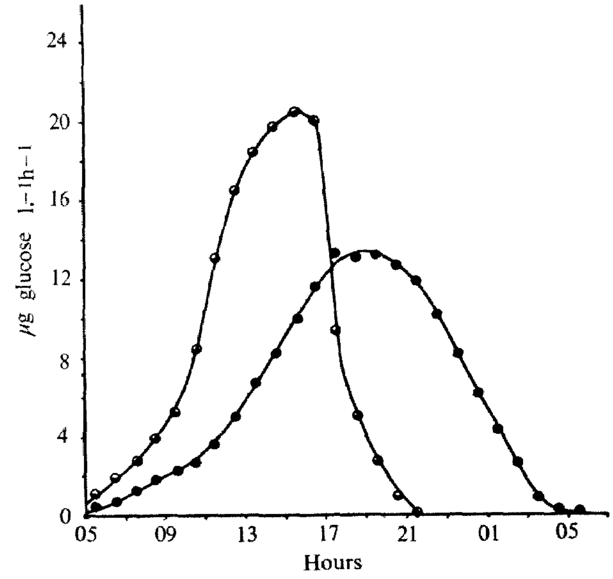

Fig. 3 Simulation experiment for phytoplankton extracellular release and bacterial assimilation. Wintergreen Lake, Michigan, July 10, 1970. ◒—◒, Extracellular release; ●—●, bacterial assimilation.

aluminium foil to ensure complete darkness and were incubated in the surface water for 34 min. After this time 20 ml. subsamples were injected into sealed absorption vessels containing 1 ml. of concentrated phosphoric acid. The *p*H of the injected sample was reduced to 1.0 so that further metabolism of glucose was stopped and all bicarbonate transferred to carbon dioxide. The carbon dioxide was allowed to diffuse into a vial containing a carbon dioxide absorbant. The radioactivity in the vial was subsequently determined by scintillation counting.

A second set of subsamples was filtered through 'HA Millipore' filters into a preservative to prevent further metabolism of glucose. The filtrate was acidified and degassed of inorganic carbon. This treated sample was then plated, dried and the radioactivity was counted. The radioactivity in the bacteria on the filter was also determined. In this way a carbon-14 radioactivity (mass) balance was obtained for each tracer assay. There were no discrepancies in the carbon-14 balance for any tracer assay.

The sum of the carbon dioxide and bacterial carbon-14 radioactivity produced per unit time was considered to be the gross or true assimilation rate of ^{14}C-glucose. Knowing the simulated extracellular release rate of glucose-C-12, the bacterial assimilation rate of glucose-C-12 was calculated for each tracer assay. The results (Fig. 3) demonstrate that a fluctuation in the extracellular rate of release of glucose is accompanied by a fluctuation in the bacterial assimilation rate of glucose. There is a phase difference in the maxima of the two rates of slightly more than 3 h. This experiment thus proves the general biological phenomenon. The initial concentration of glucose in the lake water was not known. It was assumed to be 1 μg l^{-1} for purposes of the calculation. It can be shown for this experiment, however, that the bacterial assimilation rate will oscillate even if the initial concentration of glucose was 100 μg l^{-1}. The latter value is much greater than any known concentrations of glucose in lake water.

Any substrates released by phytoplankton which have a relative utilization rate similar to glucose will produce a similar oscillation in the assimilation rate. The period of the oscillations will be 24 h and the substrate will be almost completely utilized within 24 h. A substrate that is utilized more slowly than glucose will also produce a fluctuation in the bacterial assimilation rate. The phase difference between extracellular release and bacterial assimilation would tend to be much longer. The ultimate response of the bacteria could be much more complex than in the foregoing example.

It is possible, therefore, to view the total reaction sequence of light, phytoplankton, extracellular soluble organic matter, and bacteria, as a linearly coupled fluctuating control system. In this system light intensity is a forcing environmental variable and the phytoplankton–bacteria constitute a biological response system where the coupling between phytoplankton and bacteria is mediated by a fluctuating soluble organic pool. The intensity of each response will oscillate and will be somewhat out of phase with the preceding component of the system. This sequence constitutes a basic control mechanism for bacterial development.

Such a basic control mechanism provides a basis, in part, for analysing the population development of phytoplankton and bacteria in lakes and for discerning additional control mechanisms which operate to dictate what that development might be.

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Food Chain Model for DDT Kinetics in a Freshwater Marsh

EQUATIONS of first order kinetics have been suggested as potentially suitable models for the accumulation of DDT in living organisms[1-3]. Although much has been written about the use of such models in analysing "tracer" studies[4], and in studying the fate of radionuclides in ecosystems[5,6], little has been done to construct a model to represent field data for pesticides. Knowledge of the kinetics of pesticides in ecosystems is at present insufficient for completion of the model, but we believe that this will be possible when certain problems have been solved. A full account of the field study[7] and a detailed report of the model are available[8].

The data of Fig. 1 were obtained using DDT labelled with chlorine-36 on the phenyl ring. This DDT was applied in an inert granular carrier[7] from a helicopter to an enclosed 4 acre marsh at the south-western edge of Lake Erie in July 1964, at a rate of 0.2 pounds of technical grade DDT/acre (220 g/ha). Our model assumes an exponentially decreasing rate of release of DDT from the granules into an average of about 12 inch (30 cm) of water, followed by transfer to suspended materials (chiefly phytoplankton) and various items of the biota according to equations of the form

$$\frac{\mathrm{d}y_2(t)}{\mathrm{d}t} = c_2 y_1(t) - \mu_2 y_2(t) \qquad (y_i(0) = 0)$$

where $y_2(t)$ represents DDT concentration in a given "compartment", c_2 is a "transfer coefficient", μ_2 is a rate of loss and $y_1(t)$ is the concentration of the source of DDT taken in by the given compartment. The concentration of DDT in filtered water is assumed to follow the equation

$$\frac{\mathrm{d}y}{\mathrm{d}t} = \lambda e^{-kt} - \mu y$$

where λe^{-kt} represents release from granules, and μy losses from water due to all causes. Rate constants for this equation were obtained by a nonlinear least-squares fit to its solution, neglecting the two points represented by open circles in Fig. 1. A more realistic model would assume recycling of DDT, so that releases of DDT from various components might again be taken up from the water. But such a model does not seem feasible with the available data. Codistillation of DDT with water is potentially important for the determination of the fate of DDT in an aquatic system. Some laboratory experiments have shown losses through codistillation of more than 50% of the quantity introduced within 24 h (refs. 9, 10), but we have no relevant data.

Rate constants for twenty different species were obtained, five of which seemed to fit realistically into the food chains of Fig. 1. In many cases we assumed that individual species had two compartments, one representing long-term retention and the other (a "fast" compartment; shaded areas in Fig. 1) representing transient conditions when the concentration of DDT in the water was relatively high. We assumed that the fast compartment was essentially depleted of DDT in the first 14 days after application, and used the observations on and after the fourteenth day (usually four points: 14, 30, 60 and 90 days after application) to estimate rates of loss and transfer for the long-term ("slow") compartment. Contents of the fast compartment were then assumed to constitute the difference between observations and a computed curve for the slow compartment. These differences were usually maximal either 24 or 72 h after application, so we arbitrarily assigned rates of loss which yielded corresponding maxima in a computed curve. Fast and slow compartments were added to constitute the total DDT burden of a given species. Because our parameter estimates for the fast compartment seem unreliable we suggest the use of autoradiography to study possible plant "compartments" in controlled experiments. It is quite possible that our "fast" plant compartment is, in part at least, associated with periphyton. We assume that the "slow" compartment constitutes DDT somehow bound to plant tissues, but note that the available evidence suggests DDT is not translocated by plants, so that a likely candidate for the slow compartment is the cuticle[11].

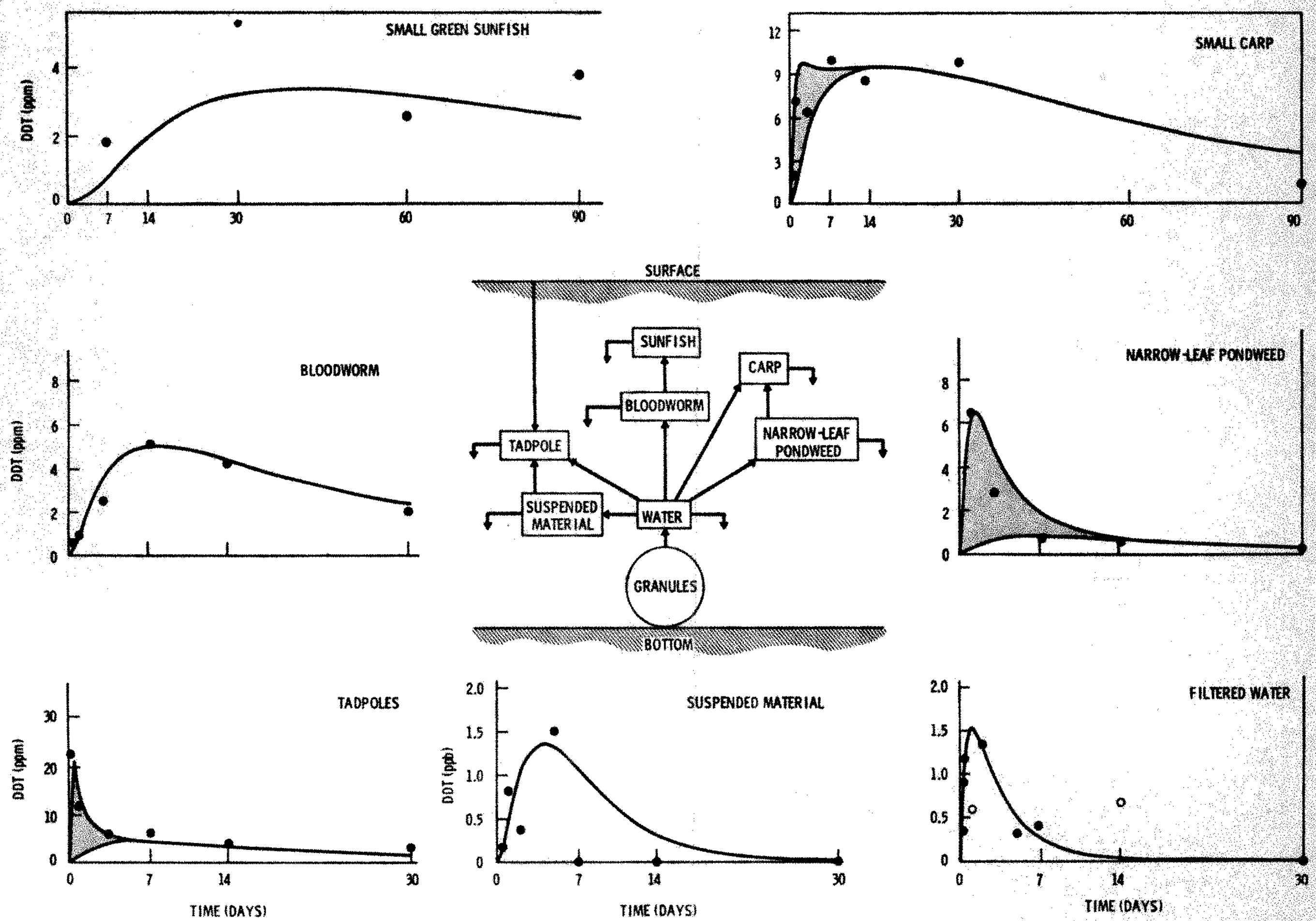

Fig. 1 Food chain model for selected items of the biota of a freshwater marsh. Plotted points represent observed concentrations of DDT at various times after application. Solid curves represent concentrations computed from the model equations. Shaded areas (carp, tadpole and narrow-leaved pondweed) represent the contribution of a "fast" compartment.

One of the puzzling outcomes of this study is that concentrations of DDT in suspended matter (largely phytoplankton) decrease below detection limits 7 days after application. A few parts per billion of DDT can appreciably reduce photosynthesis by marine phytoplankton[12], but we have no basis on which to argue for or against a similar effect in our study.

Although all ten of the plant species modelled required two compartments, it seemed that most of the six invertebrates could be represented by single-compartment models. Tadpoles contained very high DDT concentrations (23 p.p.m.) within a few hours of application, so we have assumed a fast compartment with inputs from a transient water surface concentration of DDT (probably a DDT–xylene–dust aggregation). Both carp and green sunfish had maximal concentrations of DDT of the order of 30 days after application, and so we assumed that they received most of their DDT through the food chain. An initial very rapid increase in concentrations in carp was assumed to be due to a fast compartment receiving DDT directly from the water. We have too few data to determine reliably the dominant mode of DDT uptake by fish in field conditions. Direct uptake from water has been demonstrated[13,14], and high concentrations may readily be obtained from food containing DDT[15,16]. Our observations, and others[17], suggest that maximum concentrations are associated with the food chain, but controlled experiments are needed in more or less natural conditions. A promising approach seems to be the use of differentially labelled DDT, with one "tag" in water and the other in food items—DDT labelled with carbon-14 or chlorine-36 is available. We should point out that what we call "DDT" undoubtedly includes various degradation and metabolic products (especially in the fauna). Because the phenyl ring of the chlorine atoms remains attached to all known DDT metabolites[7], we are confident that our data represent the fate of DDT and its metabolic and degradation products, but an unrealistically large effort would be required to establish relative proportions of the various constituents in time.

Our estimates of transfer coefficients and rates of loss for the long term compartments are summarized in Table 1. We would like to emphasize that the use of concentration factors depends on the maintenance of a constant level of DDT in the water. Our two compartments are effectively assumed to be of equal mass (because we simply add concentrations in the two compartments to obtain overall concentration in a given species). In equilibrium conditions, concentration (dry weight) in a given organism (y_i) is then

$$y_i = y_w \left[\frac{c_1}{\gamma_1} + \frac{c_2}{\gamma_2}\right] \equiv [y_w] \text{ [concentration factor]}$$

where y_w is the concentration in water, and c_1 and γ_1 are respectively transfer coefficients and rates of loss. The usual interpretation of a concentration factor as the ratio of concentration in an organism to that in water may thus often be misleading when applied to DDT, and reliable measurements of concentrations in water are of crucial importance. In the case of a single surface application of DDT to an aquatic system, an approximation to a dynamic model may be helpful for planning purposes. If concentration in one compartment of an organism is represented by y, then

$$y \doteq \frac{c\lambda}{k} e^{-\gamma t}$$

where c is the transfer coefficient, γ the rate of loss (Table 1), and decrease of DDT in water follows the equation

$$y_w - \lambda e^{-kt}$$

Further details and some crude estimates of λ and k are given in ref. 8. Suspended matter cannot be neglected, so that three separate measurements of water concentrations ought to be considered (a bulk water sample, suspended material and filtrate).

Table 1 Parameters of DDT Uptake and Retention by Marsh Biota

Species	Long term compartment *				
	Transfer co-efficient	Rate of loss (× 10⁴)	s.e. (× 10⁴)	Concen-tration factor †	Conver-sion factor —dry to wet weight
Plants					
Sago pondweed (*Potamogeton pectinatus*)	9.1	1.8	1	53,000 (0.98)	0.12
Curly leaf pondweed (*P. crispus*)	7.3	0.9	5	84,000 (0.98)	0.17
Narrow-leaf pondweed (*P. foliosus*)	7.5	25.0	–	7,100 (0.42)	0.11
Water milfoil (*Myriophyllum* sp.)	8.0	7.8	5	11,000 (0.91)	0.17
Bur reed (*Sparganium eurycarpum*)	3.5	5.7	2	8,900 (0.68)	0.07
Soft stem bulrush (*Scirpus validus*)	13.0	39.0	14	5,500 (0.60)	0.09
Duckweed (*Lemna minor*)	45.0	55.0	35	11,000 (0.72)	0.11
Coontail (*Ceratophyllum demersum*)	13.0	15.0	4	15,000 (0.61)	0.13
Cladophora (*Cladophora* sp.)	130.0	59.0	18	83,000 (0.24)	0.26
Bladderwort (*Utricularia vulgaris*)	14.0	12.0	0.5	22,000 (0.56)	0.10
Invertebrates					
Red leech (*Erpobdella punctata*)	77.0	16.0	–	47,000 (1.00)	0.16
Crayfish (*Orconectes immunis*)	27.0	13.0	2	22,000 (0.93)	0.23
Dragonfly naiad (*Anisoptera*)	–	7.6	7	–	0.18
Backswimmer (*Notonectidae*)	30.0	28.0	4	10,000 (1.00)	0.24
Bloodworm (*Tendipes* sp.)	42.0	17.0	2	25,000 (1.00)	0.19
Ramshorn snail (*Planorbidae*)	13.0	32.0	20	4,700 (0.89)	0.58
Vertebrates					
Carp (*Cyprinus carpio*)	–	7.8	3	–	0.23
Green sunfish (*Lepomis cyanellus*)	–	5.9	2	–	

* Coefficients expressed on a per hour basis.

† Figures in parentheses give proportion due to long term compartment.

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BOOK REVIEWS

Paradigms and Policy

Science Studies: Research in the Social and Historical Dimensions of Science and Technology. Edited by Roy MacLeod and David Edge. Quarterly. Volume 1, Number 1. Pp. 115. (Macmillan: London, January 1971.) £5.00 annually ; £1.50 each copy.

"SCIENCE," one might feebly quip, "is too serious a matter to be left to the scientists." The time has come for historians, philosophers, sociologists, economists, and the like to tell us what we are really doing and what we ought to do. The past decade is notable for the ascent into academic consciousness of a new interdisciplinary discipline—the study of science itself. *Science Studies* is to be a vehicle for the publication of scholarly articles on this subject. It is very welcome: may it flourish.

As every sociologist of science now knows, a new journal signifies the budding of a new invisible college. With active groups already established in several universities, we may anticipate rapid growth for the darling child. It is perhaps worth enquiring into its parentage and prospects.

On the distaff side, we observe the ancient scholarly house of History and Philosophy of Science, whose lineage may be traced back at least to Francis Bacon and Bishop Sprat. Here already there is no lack of journals, conferences, paradigms and pundits—not to mention perennial controversies of the kind exemplified by David Bloor's Essay Review of the Kuhn–Popper tourney. No great disrespect is intended if I suggest that this sort of thing is certainly most interesting to those interested in this sort of thing, but that it has not quite lived up to its high ideal of throwing floods of light on the scientific enterprise.

The other proud parent is sociology, whose cloud of pedantic polysyllables has begun to envelop the scientific community. Shrewdly handled, the professional headlamps of social enquiry can illuminate many features of the scholarly life—for example, the "norms" of scientific behaviour, or the means by which controversies are controlled. Unfortunately, conceptual schemes originally devised for the analysis of the role structure of the Navajo Indians are not quite adequate when applied to a tribe of astrophysicists and molecular biologists. Nor does a quick gallop through the conventional literature, as in R. G. A. Dolby's "Sociology of Knowledge in Natural Science", leave one with a 'Eureka' feeling (sorry—having experienced an *Aha-erlebnis*). J.-J. Salomon on "The *Internationale* of Science" is pleasant, but also unprofound, at the level of high-brow journalism.

Or is the brat a bastard born of practical expediency? Science costs money, and has become a decisive factor in the economic and political domain. Problems of "scientific choice", which used to be settled discreetly in the basement of the *Athenaeum*, now erupt into the public eye. Expertise on cost benefit analysis, technological forecasting, international administration and other useful arts has become essential equipment for the worldly scientist and his political allies. This is the "Real World of Science Policy" in which K. Kreilkamp sets the *Hindsight* project, and the screen on which D. J. de S. Price projects his logistic extrapolations of the exponential growth curve, with typical numeracy. It is also the arena of moral concern and political ideologies described so vividly and appositely by P. G. Werskey in his historical account of "British Scientists and 'Outsider' Politics, 1931–1945".

The genesis of this journal therefore presents splendid opportunities for hybrid intellectual vigour. Let us cross Kuhn with Price and put numbers into the paradigms. Polanyi's idealism and Werskey's realism would protect Mertonian sociology from the fungus of academicism. A few Popperian genes might mask some of the lethal mutations of neo-Marxist social relevance—and so on. Above all, let us have more from active scientists—men and women who know from experience the joys and pitfalls of the search for a philosophy of nature. The editorial board is too heavily loaded with professional "Science Studies" scholars. What about Blackett and Medawar, Zuckerman and Weisskopf, Kothari and Salam, who have made science policy themselves and understand it quite as well as the academic analysts and commentators? "Science Studies," one might retort, "are too serious a matter to be left to the Students of Science."

My real fear is that the infant will be fattened on a pappy diet of "normal" philosophy, history and sociology, spiced with jolly little enumerations of the trees of citations in molecular biology. It should be brought up as a spartan, to digest hard lumps of logic and linguistics, developmental psychology and economic statistics, and to strive manfully with such invincible opponents as scientific education, technological responsibility and national development. Many clichés of the conventional wisdom are waiting to be challenged, and many heretical concepts are demanding to be adopted. "Science" is a fit topic for the most diverse scholarly techniques, but the mere fact of its "importance" is not enough to justify flabby thought and implausible speculation. I hope, therefore, that the editors will take their duties seriously, and will give this journal a reputation for sharp-minded, diverse and original work on which we may lean with some confidence in the exercise of our communal profession.

JOHN ZIMAN

Costing Education

An Introduction to the Economics of Education. By Mark Blaug. Pp. xviii+363. (Allen Lane, The Penguin Press: London, November 1970.) £3.50.

IT is interesting to ask whether or not education and science contribute to economic growth. Put like that, of course, the question is absurd, but it can be broken up into meaningful parts. To these much more specific questions, specific answers can be given, on the basis of extremely detailed studies of the content, structure and relevance of particular bits of education and science to actual situations. Of course, such answers will be based on a general structure of ideas. Natural scientists may suspect, but they probably do not usually know, that the structure of ideas in such disciplines as economics, history, and (say) textual criticism is different from—though allied to—the structure and organization of thoughts to which they are accustomed in their own disciplines, though, of course, it is incorrect to believe that there is a single general corpus of "science" that can be teased out from the individual disciplines of biology, physics and so on. Economics is not a science in the sense in which physics is; and those who assert that it is—the advocates of so-called "positive" economics—are as partisan as (though usually less frank than) those who take a more complex view of what their discipline actually is.

In education—itself a collection of highly disparate activities—economists can seek to analyse what has been spent, and what its consequences in the economic sense have been, and they can also ask "ought" sorts of questions—what ought to be spent, and what would be the relevant range of criteria that might be brought to bear on such a question. Though the "is" questions are far from simple, the "ought" questions are extraordinarily complex, shot through with the social, political, ethical and cultural issues that necessarily dominate education and research.

One kind of "ought" answer has been manpower planning. It is fairly clear that, for the most part, manpower planning as a general strategy is a poor guide to educational planning. It dominated British university expansion in the 1960s. The results are fairly obviously undesirable. The physical sciences and technology have been disproportionately expanded, but this is not the direction of student choice. Research has been far too lavishly supported, but there are not enough jobs for the graduates. Britain combines one of the world's highest research efforts with one of the lowest rates of economic growth. All this is the result partly of the scientific lobby, and partly of a most inadequately studied assertion of a relationship between scientific research, trained scientists, and economic growth. Mark Blaug deals effectively with this sort of error in his new introductory textbook, though (to be honest) it is not an error that has been undealt with before.

What is more doubtful, however, is whether his chosen solution is any more help. Could we get a guide to the "correct" allocation of resources to education and science from the market, or from a paradigm of the market? Blaug is one of those economists (chiefly from the United States and its offshoots) who believe that economics is about markets. This so-called neoclassical view of economics is not shared by a great many people, and it seems to me to be curiously inapposite to the analysis of what are, for the most part, services that in most countries fall emphatically into the public sector of the economy. There are grounds, too, for believing that the answers derived from questions posed by such a mode of reasoning will be systematically misleading, for the market mode of reasoning necessarily asserts that there is (under competitive conditions) a set of prices, including the differential earnings of different grades of labour, which have some significance as guides to priorities. For those to whom price does not seem to play so large a role, and who are concerned with other questions, this will seem to lead to different answers to different questions.

There is, too, ground for further criticism of this volume. It seems to lack the intimate knowledge of the chosen field—education—that is desirable in a commentator. It is easy to hand down prescriptions from a medical encyclopaedia if detailed clinical inspection of the patient is deemed unnecessary.

JOHN VAIZEY

Fossil Records

The Elements of Palaeontology. By Rhona M. Black. Pp. 339+4 plates. (Cambridge University: London, December 1970.) 4.50 boards; £2.25 paper.

THE reception of this book is bound to be controversial. Potential buyers are well advised to turn from the comments on the jacket to the words of the preface before assessing it. Here it clearly states that the book's objective is to introduce all the principal groups of invertebrate fossils and an outline of the palaeontology of the vertebrates and plants to students who require a knowledge of a wide field in palaeontology at an introductory level. The preface continues: "Some emphasis is given to biological aspects of palaeontology . . ." whereas the dust jacket misleadingly states: "Particular attention is given to the biological aspects of palaeontology." Similarly the dust jacket leads the reader to believe the book is the palaeontological panacea for students in schools, colleges and universities; a claim which is not made in the preface and which cannot be substantiated. Thus the author's intentions have resulted in a beautifully illustrated palaeontological textbook of the classical British school. As that it could be welcomed and praised for its breadth of scope and general high quality of its numerous photographs.

It is particularly useful in that the usual range of creatures is illustrated along with photographs of diatoms, antiarchs, coccoliths, bryozoan zoecia, and the alga *Solenopora,* all of which are usually ignored at this level. The layout is orderly. The invertebrate phyla are systematically treated under headings of morphology, mode of life, and geological history. A short technical description of characteristic British genera and their stratigraphical range is given and the chapters are closed with a list of technical terms. The index is reliable.

But on close inspection the labelling of diagrams leaves something to be desired, for example, throughout figure 130 on graptolite structures, the plural form is used yet only one theca is marked in each instance; the diagrams of the corals are particularly disappointing. The book's weaknesses lie in its treatment of the biological and evolutionary aspects, preservation, and the extremely limited suggestions for further reading and reference.

JULIA A. E. B. HUBBARD

Problems in Childhood

A Neuropsychiatric Study in Childhood. By Michael Rutter, Philip Graham and William Yule. (Clinics in Development Medicine Nos. 35/36.) Pp. vi+272. (Spastics International Medical in association with Heinemann Medical: London; Lippincott: Philadelphia, 1970.) £3.75.

THERE are few trickier problems than that presented by the child with a behaviour disorder—and behaviour disorders are very common in children. They range from the serious conditions associated with mental retardation or epilepsy to many milder disorders, such as bed-wetting and anti-social behaviour at school. The neurologist may diagnose "minimal brain damage" while the psychiatrist thinks in terms of early maternal deprivation. The viewpoints of parent and teacher are different again. The authors of this book are well known as leading investigators in this field and they have performed a valuable service in producing an eminently practical book, clearly written in chiefly non-technical language and giving a sensibly balanced view. The book is well produced, well illustrated, and it maintains a high standard throughout. It can be recommended warmly to all who are looking for practical guidance in the subject.

DEREK RICHTER

Control of Malaria

Chemotherapy and Drug Resistance in Malaria. By W. Peters. Pp. xvi+876. (Academic: London and New York, December 1970.) £13.00.

TWENTY years ago the appearance of anopheline mosquitoes resistant to residual insecticides spurred the World Health Organization into a programme designed to eradicate malaria from the world. Resistance of vector parasite to drugs seemed to pose no threat to the success of the campaign. Today, most vector mosquitoes remain susceptible to DDT.

It would be an exaggeration to say that drug resistance in malarial parasites has been the principal cause of slow progress towards the eradication of malaria, but the increasing insusceptibility of *Plasmodium falciparum* to chloroquine in South America and South-East Asia is serious—both for malariologists faced with the prospect of foci of infection due to resistant parasites, and for the clinician who may find that half his patients suffering from falciparum malaria are not cured by the standard treatment with chloroquine.

Professor Peters's book could not have appeared at a more opportune moment though topicality has disadvantages. Many of us require up to date information on this subject, but changes are occurring so rapidly that any review aiming at completeness soon becomes obsolete. Originally, the book set out to review all important work on the subject up to the end of 1968 ; but, to deal with later work up to the autumn of 1969, an addendum of 36 pages reviews 240 more recent papers. This arrangement, though demanding constant reference to the addendum, succeeds in keeping the book up to date. Peters assures us that the tempo of malaria research now shows signs of slackening ; should one be ashamed to admit a feeling of relief?

Two factors combine to make this book stand out above similar reviews of subjects of current scientific importance. The first is Peters's own career. For many years he was a "wet-foot" malariologist in some of the most difficult countries in the world, including Nepal, Liberia and New Guinea. During the last ten years his work has been in biological laboratories in Switzerland and Liverpool. There can be few scientists who can write with such authority, both on basic research and on its application in the control of a disease that afflicts "poor people in obscure places".

The second factor that makes this work outstanding is the quality of the language. There are a few review books of this type that are a pleasure to read. Davidson and Passmore's *Human Nutrition and Dietetics* is one ; Peters has produced another. The clarity of the language makes the matter digestible and the frequent happy phrasing adds a spice of enjoyment. This is particularly true of the introduction, which summarizes the aims of the book and gives the historical background of chloroquine resistance.

The early chapters deal with basic information about the malaria parasite, the host–parasite relationship and the techniques employed in evaluating drug response both in man and animals. The principal part of the book discusses systematically, drug by drug, experimental resistance, both in the laboratory and its practical application in human malarias. Special aspects of drug resistance, described separately, include the influence of drug combinations, entomological, immunological and genetical aspects. The final chapters present the practical effects of drug resistance in the field.

The references and subject indices, essential in a book of this nature, are of a high standard. For the field worker a place index would have been useful to give easy access to information about resistance in the country with which he is concerned. It is not easy to find this information quickly in the subject index. The only other criticism is of the title itself. This is a definitive work on drug resistance rather than on the chemotherapy of malaria. But these are minor points to make about such an excellent book.

It covers such a wide field that the impression of the reader will tend to reflect his own interests. I was particularly interested in the story of the downfall of "infallible" chloroquine as a weapon against *P. falciparum*, the critical examination of methods of evaluating this failure in the field and in methods of preventing or eliminating drug resistance. The absence, so far, of chloroquine resistance in Africa is of vital interest. This could be due to less intense use of the drug than in South-East Asia or South America, but Peters holds out some hope of other explanations.

Peters gives several examples of apparent drug failure being really due to failure of the patient to swallow the tablets. This practical difficulty was probably the principal cause of the failure of the drug trial at Kankiya, which had convincing mathematical arguments in its favour.

The vital problem of the place of drugs in the future of malaria control emphasizes the value of Peters's experience. New drugs are required and must be evaluated in the laboratory, but it requires a malariologist to assess their practicability as a control measure in the field. Both aspects are combined in this splendid book.

M. J. COLBOURNE

Wasp Biology

The Wasps. By Howard E. Evans and Mary Jane West Eberhard. Pp. vi+265. (University of Michigan: Ann Arbor, November 1970.) $3.45 paper; $7.95 boards.

THIS book embraces a very wide and richly varied field of wasp biology. An introductory chapter briefly describes the principal groups of wasps, their probable evolution, their representation in North America and their importance to man. Whereas some wasp species are regarded as pests because of their habit of raiding honeybee colonies, others have been used in the biological control of plant pests and some species of social wasp in Brazil and Mexico store sufficient nectar to make exploitation by man worth while.

Chapter 2, on the natural history of wasps, is the longest chapter and is in many ways one of the most interesting. It gives a comparative account, together with the underlying evolutionary themes, of a number of biological topics that are common to wasp species. These topics include the egg stage, larval and pupal stages, adult feeding and food, predatory behaviour, prey carriage and orientation to the nest. The amazingly diverse nests and types of nesting behaviour of solitary wasps are the subjects of Chapter 3. Many of the examples of nesting behaviour that are quoted are of great interest to students of animal behaviour; for example, several species of *Ammophila* use a pebble as a tool to hammer down the material filling the entrance to a burrow, and certain species of ***Sphex, Bembix*** and ***Philanthus*** dig small holes or accessory burrows which divert the attention of parasites away from the real entrance to the nest and which are reminiscent of the false entrances of Neolithic burial mounds. In fact, the contribution that wasp studies have made to the field of animal behaviour is quite remarkable. Nest building behaviour, prey collection, nest provisioning and nest site learning provide classical illustrations of sequential behaviour patterns, performed in the presence of appropriate releasers, which often exhibit a certain degree of flexibility. These and many other fascinating subjects, including pseudo-copulation with orchids which mimic female wasps, are lucidly and enthusiastically portrayed.

The next two chapters are concerned with the social wasps, their colony initiation, growth and termination, nest architecture, foraging, brood care, division of labour and communication between individuals within a nest, caste determination, mating and hibernation. Finally, Chapter 7 describes many of the wasps, flies and beetles that are parasitic on wasps and their nests, and finishes with an evaluation of the survival value of wasps' aposematic coloration.

The evolutionary backbone running through this book reaches its climax with a discussion of the origins of social life in the Hymenoptera. Because ants and bees are believed to have come from wasp-like ancestors, the wasps may hold the key to this interesting problem. The principal steps in the evolution of wasps' nesting behaviour are traced, ending with communal living, prey maceration and adults feeding larvae other than their own. The recently propounded theory on the part which the haploid–diploid mode of sex determination has played in facilitating sociality among the Hymenoptera receives special treatment.

It is, of course, possible and profitable to compare the behaviour of wasps with that of other Hymenoptera, and the parallels between wasp and bee behaviour and the associated problems are often particularly striking. The current trend in the use of trap nests to investigate solitary wasps and bees has focused interest on the common problems of development and emergence of insects produced in a linear series of cells. Indeed, even the correct orientation in their cells of the pupae of both solitary wasps and honeybees seems to depend upon similar sensory cues. Solitary bees are renowned for their specific foraging preferences and most solitary wasps also specialize in a particular kind of prey, but, in general, social wasps, like social bees, have lost their host specificity, no doubt because they are not limited to one brood generation and a brief foraging period.

The direct transfer of food between the members of a social insect colony was first demonstrated for wasps, and the realization of its extensiveness and importance in ants, bees and termites as well as wasps has allowed many important advances in our understanding of insect societies to be made. When a wasp larva receives an appropriate signal from an adult it exudes a drop of fluid from its mouth which the adult imbibes. Although this behaviour (trophallaxis) has long been known, the value, if any, of the fluid to the adult is still a matter of controversy. Indeed, as the authors point out, despite the large amount of current research on wasps and other social insect colonies we still do not know precisely how the colonies are organized.

There is a suggested reading list of 10 publications. Although 40 authors are mentioned in the text the sources of their work are not given, but nevertheless the authors are to be congratulated on bringing together such a large amount of fascinating information and presenting it in an eminently readable manner.

JOHN B. FREE

Sounds Submerged

Underwater Acoustics. By Leon Camp. Pp. xi+308. (Wiley-Interscience: New York and London, November 1970.) £8.25.

THE origin of this book was an intensive sixty hour lecture course at the University of California given to practising engineers with various academic backgrounds. Because the underwater acoustics field is very broad, the authors admit they had difficulty selecting material so as to keep the book to a manageable size. On this point, the authors are to be congratulated. Their coverage is quite adequate for either final year undergraduates or graduate engineers just entering the field, for whom the book is presumably intended.

Introductory chapters deal with the mechanics of vibration, and introduce the ideas of complex number notation, phase, resonance and selectivity. Wave and ray acoustics are described in detail, together with various types of transducers and array radiation patterns. The analysis of some simple sonar situations and the use of matched filter and signal processing techniques conclude the text.

Unfortunately there are many errors in the book, and while many of these are easily spotted (equations dimensionally incorrect), readers may find the mistakes irritating and so lose confidence in the authors' integrity. It is sad that most of the errors are due to poor editing and careless proof reading.

For a book meant for students new to the underwater acoustics field it fails to present the material in a readable manner. Emphasis is given to mathematical dexterity, without explaining the meaning of many equations. For example, when the circular locus of a particular ray path is derived, the radius of curvature is given as $-Co/g$, where Co is a velocity and g a velocity gradient. There is no explanation of why the radius of curvature appears to be negative and inconsistencies in an associated diagram make the situation even more confusing.

Underwater acoustics involves the disciplines of acoustics, mechanics, and electricity, and notation conventionally used in one of these disciplines often has a completely different meaning in the others. The authors have used the notation applicable to the discipline being discussed at a particular point, and this can be very confusing, especially as no list of symbols is available except for those pertaining to one chapter. Thus it is impossible to use the text as a reference book, for time has to be spent searching for the meaning of symbols.

The last two chapters on sonar systems and signal processing include material fresh to most texts on the subject. Apart from these chapters, the book adds nothing to the range of similar books currently available.

D. J. CREASEY

Luminescent Molecules

Fluorescence Analysis: a Practical Approach. By Charles E. White and Robert J. Argauer. Pp. x+389. (Dekker: New York, September 1970.) \$18.75; £8.90.

MOST molecules absorb light somewhere in the ultraviolet/visible/infrared region of the electromagnetic spectrum and therefore absorption spectrophotometry in solution is probably the most used analytical technique for the determination of a great number of substances. Absorption bands are broad, however, and chemically similar substances have overlapping spectra, which makes the determination of one substance in the presence of others extremely difficult. Nevertheless, very small differences in molecules which scarcely affect the absorption spectrum can cause quite profound changes in the stability of the electronic state to which the absorbing molecule is promoted by absorption radiation. These molecules which have stable excited states are usually capable of some form of luminescence. Because only a few molecules fluoresce, the selectivity of fluorescence analysis is usually much superior to absorption analysis. In addition, fluorescence analysis is almost invariably more sensitive for reasons which need not be discussed here.

Fluorescence analysis has, however, for inexplicable reasons never achieved much popularity in the Western world, though other countries, particularly the USSR, seem to have used it to good effect much more extensively. More recently the twin problems of "source scatter" and "quenching", which quite unrealistically seem to have turned so many potential users against the fluorescence technique, have been more fully appreciated as relatively minor in importance, and increasing use is now being made of this method of analysis.

This book by White and Argauer gives a fairly full and detailed account of the practice of fluorescence analysis in a modern laboratory. The authors point out that there are many theoretical treatments of fluorescence phenomena, and after citing some of these they get down to their subject with commendable vigour. Instrumentation is reviewed in a chapter which may unfortunately become dated rather quickly if the topic continues to grow at its present speed, and this is followed by a very fine exposition of the correction of excitation and emission spectra—one of the best accounts of this topic that I have seen. Subsequent monographic chapters deal with fluorescent metal chelates, quantitative methods, fluorescent indicators and the application of spectrofluorimetry to separation techniques such as chromatography and to agricultural problems. Special contributions are then made on the applications of fluorescence to the study of proteins and amino-acids, polynuclear aromatic hydrocarbons and other organics and, in particular, vitamins and steroids. The phenomena of chemiluminescence, X-ray fluorescence and atomic fluorescence (wrongly labelled as "resonance" in the latter instance) are discussed usefully, and finally there is a good account of clinical fluorimetric procedure.

T. S. WEST

CORRESPONDENCE

Responsibility in Science

SIR,—*Nature*'s editorial (**229**, 513; 1971) on BSSRS, the British Association, and the problems of science and society ignores one of the crucial differences of approach between the two organizations.

Nature concedes that there is "no harm" in examining the social problems brought about by science, and adds that "there is even a need that public attention should be drawn to some of these issues". This demands, however, more than the occasional attention of a few "sensible" and "sober" individuals. We in BSSRS are concerned with analysing the values of modern science, the relationships of science with society, and the ways in which these relationships can, where necessary, be changed. And unlike *Nature*, or, apparently, the British Association's council, we do not feel it possible or desirable to divorce the ethical problems of science from the processes of "radicalization of science".

We do not see our role, as *Nature* seems to, as that of an "enlightened pressure group". To present packaged solutions to complex social problems is the type of élitist decision-making we are trying to avoid; instead of conventional minority pressure group politics, we are concerned to create a climate in which socially irresponsible decisions are confronted by an informed and active public opinion.

We offer proposals for policy where these are relevant, and have already done so over CS, herbicides, sponsored research in universities, and the dumping of radioactive waste. But this is secondary to the main task, that of analysis and criticism through which we can mobilize the social conscience both of the scientific community and of society in general.

Yours faithfully,

PETER CHAPMAN
DAVID DICKSON
SHIVAJI LAL
JERRY RAVETZ
HILARY ROSE
STEVEN ROSE
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Announcements

Miscellaneous

THE inaugural meeting of the Lysosome Club was held on January 23, 1971, and Dr A. Allison, Dr J. Dingle, Professor T. Slater, Dr L. Bitensky and Dr S. F. Contractor were elected to the committee for 1971.

The aims of the Club are to bring together informally scientists working in the field two or three times a year, with one meeting in London and others in the provinces. Any scientist working in this field who would like to join in the activities of the Club should write to the honorary secretary, Dr S. F. Contractor, Charing Cross Hospital Medical School, 62 Chandos Place, London, WC2, enclosing the membership fee of £0.50.

ERRATUM. Due to an administrative error the penultimate paragraph was unfortunately omitted from Professor W. S. Bullough's article "The Ageing of Mammals" last week (*Nature*, **229**, 608; 1971). The paragraph was as follows:

"As Comfort has pointed out, the key to the problem of prolonging the active life of man lies in the understanding of the *basic* mechanism of the ageing process, and the advantage of the present theory is that it is immediately open to an experimental approach. A technique now exists for manipulating the duration of mammalian life in a reproducible manner using only normal physiological means. This opens the way for a study of the causes and consequences of the prolongation of life in laboratory mammals and ultimately in man; it has been the lack of such a technique that has for so long prevented any rational study of the biology of mammalian ageing. It is also obvious that even if the present theory should prove to be wrong, the exploitation of this technique may enable the truth to be reached."

British Diary

Monday, March 8

Communication of Objectives—Reconciling the Interests of the Organization and the Engineer (5.30 p.m.) Dr D. Pym, Institution of Electrical Engineers, at Savoy Place, London WC2.

"Ford Commuter"—Electric Urban Vehicle (6.30 p.m.) Mr T. K. L. Dobedoe and Mr R. F. Robbins, Institution of Electrical Engineers, London Graduate and Student Section, at Thames Polytechnic, Wellington Street, London SE18.

Recent Progress on Semiconductor Microwave Sources (2 p.m. colloquium) Institution of Electrical Engineers, at Savoy Place, London WC2.

Tuesday, March 9

Air Conditioning for Human Comfort (7.30 p.m.) Mr J. Bruce, Society of Environmental Engineers, in the Mechanical Engineering Department, The University, Birmingham.

Carbon Black in Coating Application—Dispersion and Formulation Techniques (7.30 p.m.) Mr L. A. Tysall and Dr D. H. Shearer, Oil and Colour Chemists' Association, at the Griffin Hotel, Boar Lane, Leeds.

Guided Electromagnetic Waves (6.30 p.m.) Professor H. M. Barlow, FRS, Institution of Electronic and Radio Engineers, at University College London, Gower Street, London WC1. (Seventh Clerk Maxwell Memorial Lecture.)

Regulation of Enzyme Synthesis by Phytochrome (5.30 p.m.) Professor H. Mohr, University of London, in the Anatomy Theatre, University College London, Gower Street, London WC1.

Richard Owen, First Director of the Museum (6.30 p.m.) Dr M. Rudwick, British Museum (Natural History) and the Victorian Society, in the Lecture Hall, British Museum (Natural History), Cromwell Road, London SW7.

The Anatomy of the Organ of Voice in Some Genera of Anatidae (Aves: Anseriformes), Dr R. W. Warner; **Wild World,** Dr J. H. Sparks (special film on deer); **The Seals of Macquarie Island** (film, CSIRO Australia) (5 p.m.) Zoological Society of London, at the Zoological Gardens, Regent's Park, London NW1.

The Flow of Information in a University (1.20 p.m.) Professor H. Kalmus, University of London, in the Botany Theatre, University College London, Gower Street, London WC1.

Wednesday, March 10

Aspects of Military Defence Communications: Past and Future (5.30 p.m.) Mr J. R. Mills, Institution of Electrical Engineers, at Savoy Place, London WC2.

Chemical Microscopy—The Overlooked Technique (2.30 p.m.) Society for Analytical Chemistry, at the University, Birmingham.

Modernization of Shortwave Transmitting Stations (6 p.m.) Mr C. MacKenzie, Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

Starting Methods for Reversible Generator/Motor Units Employed in Pumped Storage Stations; and An Investigation into Damping Torque Coefficients and Stability of a Two Synchronous Machine System Employed in Synchronous Starting (5.30 p.m.) Dr T. J. Hammons and Mr J. Loughran, Institution of Electrical Engineers, at Savoy Place, London WC2.

Stereophonic Broadcasting (7 p.m.) Dr G. J. Phillips, Institution of Electrical Engineers, at the SEB, 1 Woodstock Road, Yarnton, Oxford.

The Origin and Publication of some Important Scientific Books and Papers (1 p.m. general discussion) Royal Institution, History of Science Discussion Group, at 21 Albemarle Street, London W1.

The Problem of Differentiation: A New Approach (5.30 p.m.) Professor H. Mohr, University of London, in the Botany Theatre, University College London, Gower Street, London WC1.

The Victoria Line (6.30 p.m.) Mr V. H. Smith, Institution of Electronic and Radio Engineers, at the Central Library, Romford, Essex.

The Work of the Alkali Inspector (8 p.m.) Mr E. T. J. Fuge, Society for Analytical Chemistry, jointly with the RIC, at Teesside Polytechnic, Borough Road, Middlesbrough.

Thursday, March 11

Electromagnetic Waves. X-ray Diffraction (1 p.m. films) Royal Institution, at 21 Albemarle Street, London W1.

Inorganic Pigments (7 p.m.) Mr R. W. Batchelor, Colour Group (Great Britain), at the North Staffordshire Polytechnic, Stoke-on-Trent, Staffordshire.

Linear and Incremental Actuators (5.30 p.m. discussion) Institution of Electrical Engineers, jointly with the I.Mech.E., at Savoy Place, London WC2.

Stereo Transmission (7.15 p.m.) Dr G. J. Phillips, Institution of Electrical Engineers, at Aylesbury College of Technology, Aylesbury, Buckinghamshire.

The Determination of Prophylactics in Feeding Stuffs (6.30 p.m.) Mr R. E. Weston, Society for Analytical Chemistry, at Liverpool Polytechnic, Byrom Street, Liverpool.

Superplasticity (7 p.m.) Professor R. B. Nicholson, Liverpool Metallurgical Society, in the Department of Metallurgy and Materials Science, The University, Liverpool.

The Anti Scientific Revolution (7.30 p.m.) Mr John Wren-Lewis, H. G. Wells Memorial Lecture, in the Old Chemistry Department, Imperial College, Imperial Institute Road, London SW7.

Friday, March 12

Application of Time-resolved Mass Spectrometry to Gas Phase Flash Photolysis (1 p.m.) Dr D. Price, Royal Institution, Photochemistry Discussion Group, at 21 Albemarle Street, London W1.

Concorde (9 p.m.) Sir George Edwards, FRS, Royal Institution, at 21 Albemarle Street, London W1.

Molecular Sieve Chromatography (2.30 p.m.) Mr D. M. W. Anderson, Society for Analytical Chemistry, Chromatography and Electrophoresis Group, at Derby and District College of Technology, Derby.

Review of Transformer Noise Suppression and Vibration Isolation (5.30 p.m. discussion) Institution of Electrical Engineers, at Savoy Place, London WC2.

The Interior of the Earth and Moon (4.30 p.m.) Professor Frank Press (Harold Jeffreys Lecturer), Royal Astronomical Society, at the Scientific Societies Lecture Theatre, 23 Savile Row, London W1.

Saturday, March 13

Expedition Iceland (3.30 p.m.) Mr David Stanbury, Inner London Education Authority, at the Horniman Museum, London Road, Forest Hill, London SE23.

Monday, March 15

A Behaviourally Testable Theory for Belief and Preference (5.30 p.m.) Professor R. B. Braithwaite, British Society for the Philosophy of Science, in the Joint Staff Common Room, University College London, Gower Street, London WC1.

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[1] Sargent, W. L. W., and Searle, L., *Astrophys. J. Lett.*, **162**, L155 (1970).
[2] Fraenkel-Conrat, H., in *Comprehensive Biochemistry* (edit. by Florkin, M., and Stotz, E. H.), **7**, 75 (Elsevier, Amsterdam, 1963).

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